Коммуникация:

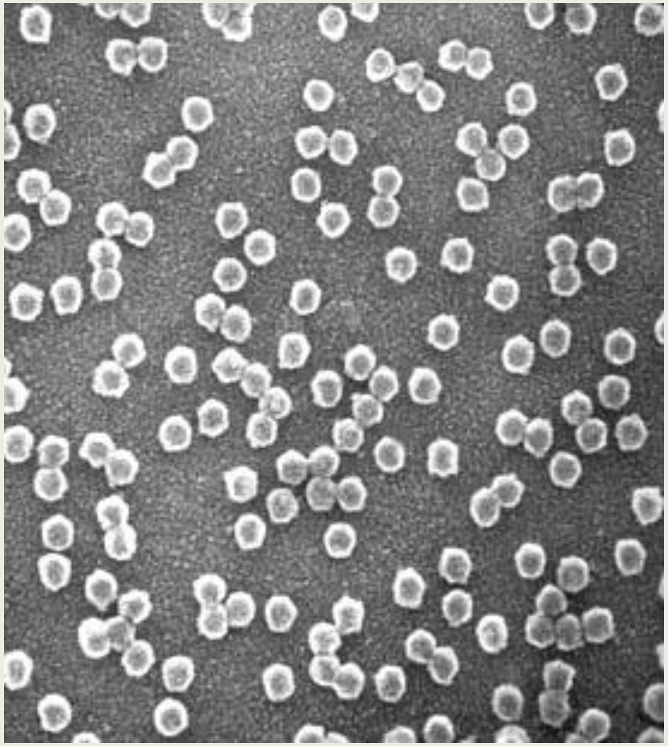
клетка-хозяин ← → внутриклеточный паразит (вирус)

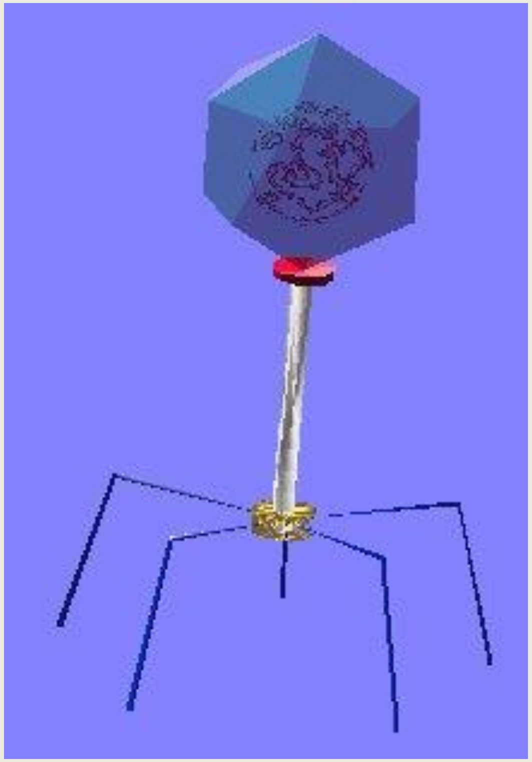
с/к «Межклеточная коммуникация»

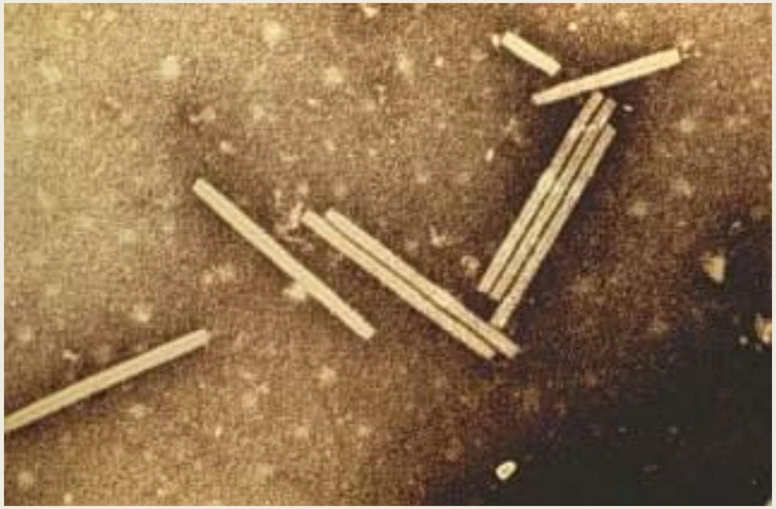
Лекция 10

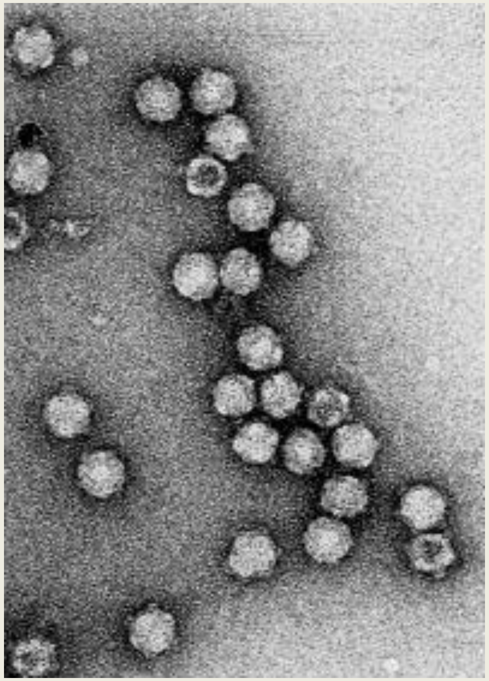
Взаимодействия

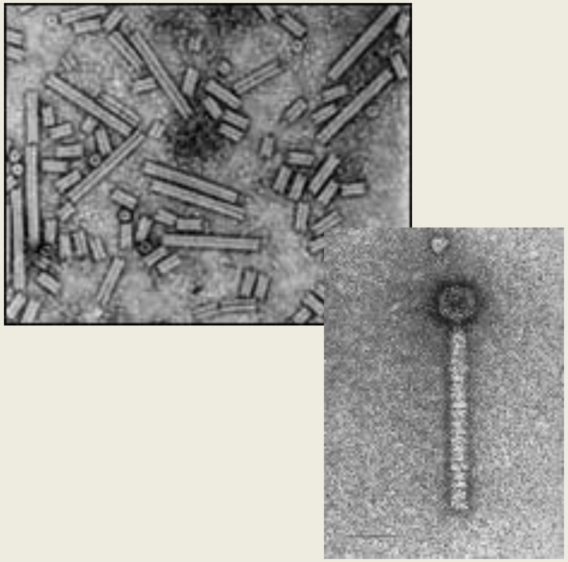
- **Клетка бактерии - бактериофаг**
- **клетка животных – вирус**
- **клетка растений - вирус**

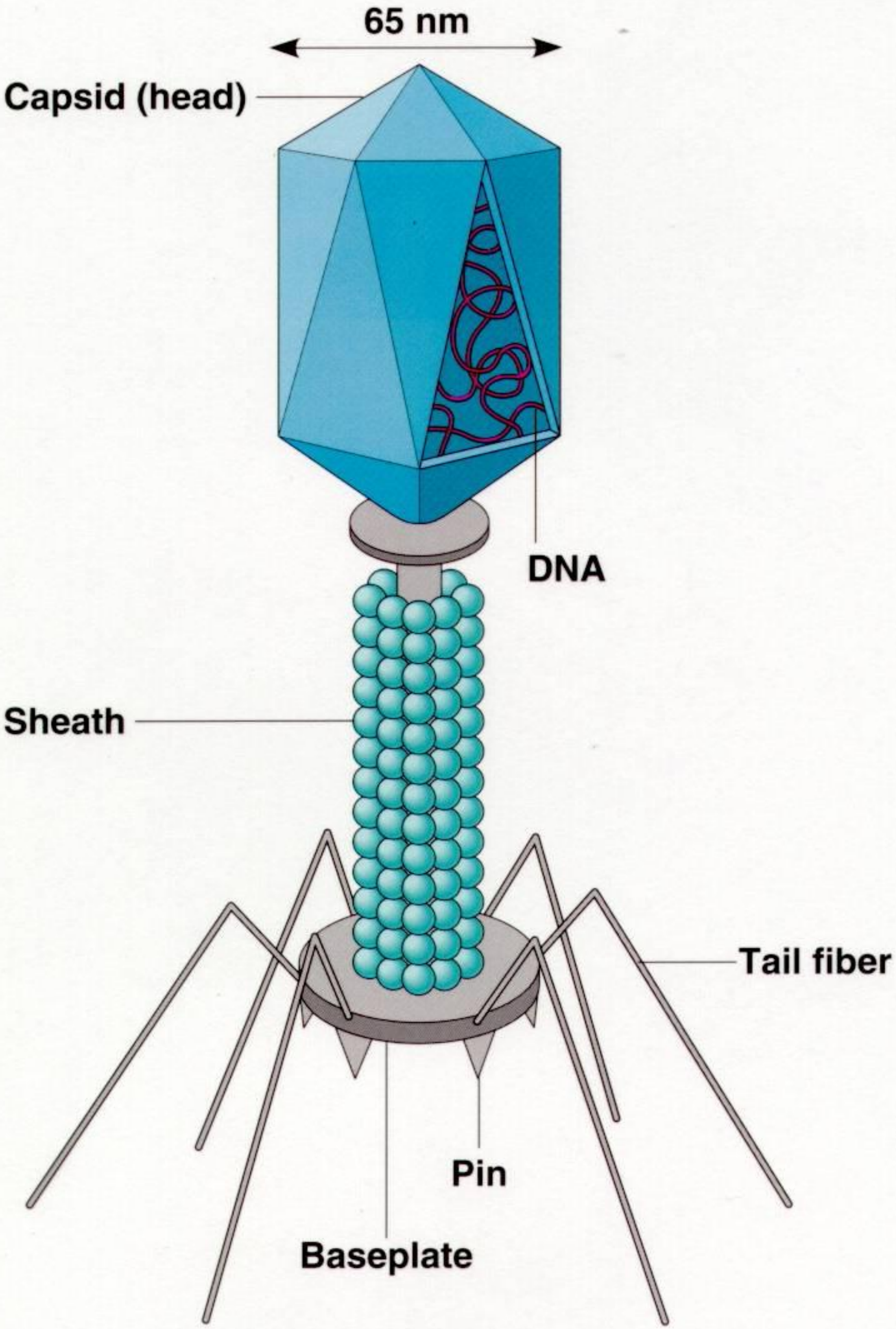











65 nm
Capsid (head)
DNA
Sheath
Tail fiber
Pin
Baseplate

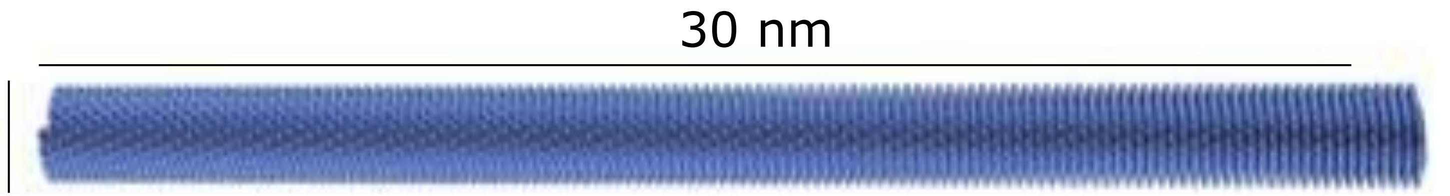
Спиральная симметрия:	Изометрическая – икосаэдр (20 плоскостей):
палочковидные или нитевидные НК скручена в спираль за счет связывания белков параллельно с синтезом НК Периодичность связывания определяет характер спирали Связи НК-капсид электростатические	сферические и сферические с хвостом НК конденсирована в «конверте». Связи с капсидом слабее, чем у палочковидных. Периодичность найдена только в некоторых вирусах (РНК-сод.) Связи НК-капсид электростатические и Ван-дер-Ваальса

ТИПЫ СИММЕТРИИ КАПСИДОВ

Биол. смысл субъединичной структуры капсида

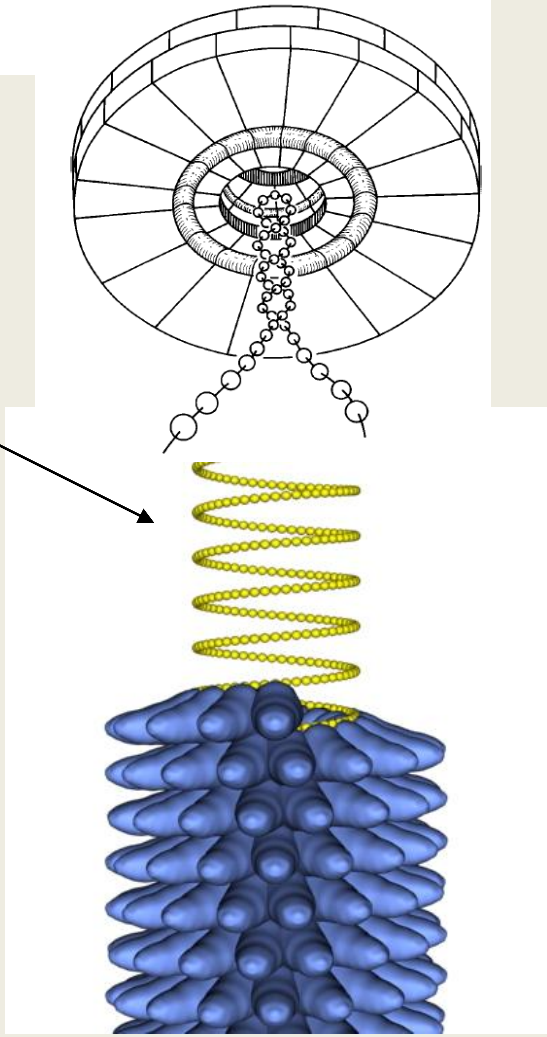
- НК может кодировать белок массой не более 15% своего веса (необходимость экономии генет.материала)
- Самосборка идет как правило из блоков, где каждый из промежуточных ансамблей – затравка для следующего
- Более высокая точность синтеза, если небольшой белок
- Неправильную субъединицу легко заменить
- Энергетически более выгодно формировать периодическую структуру с большим числом контактов между малыми субъединицами

STRUCTURAL FEATURES OF TMV

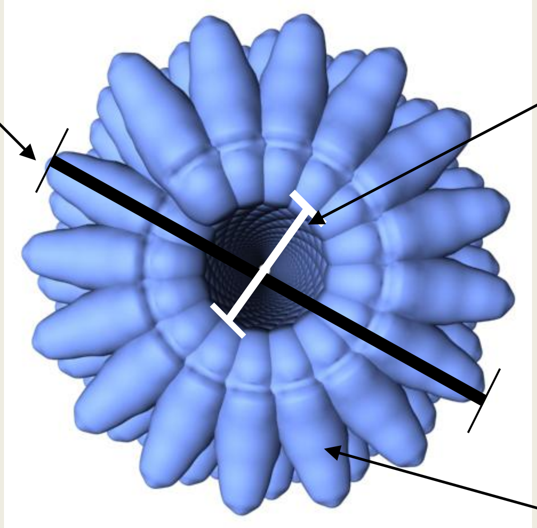


CAPSID

Helical symmetry



RNA genome

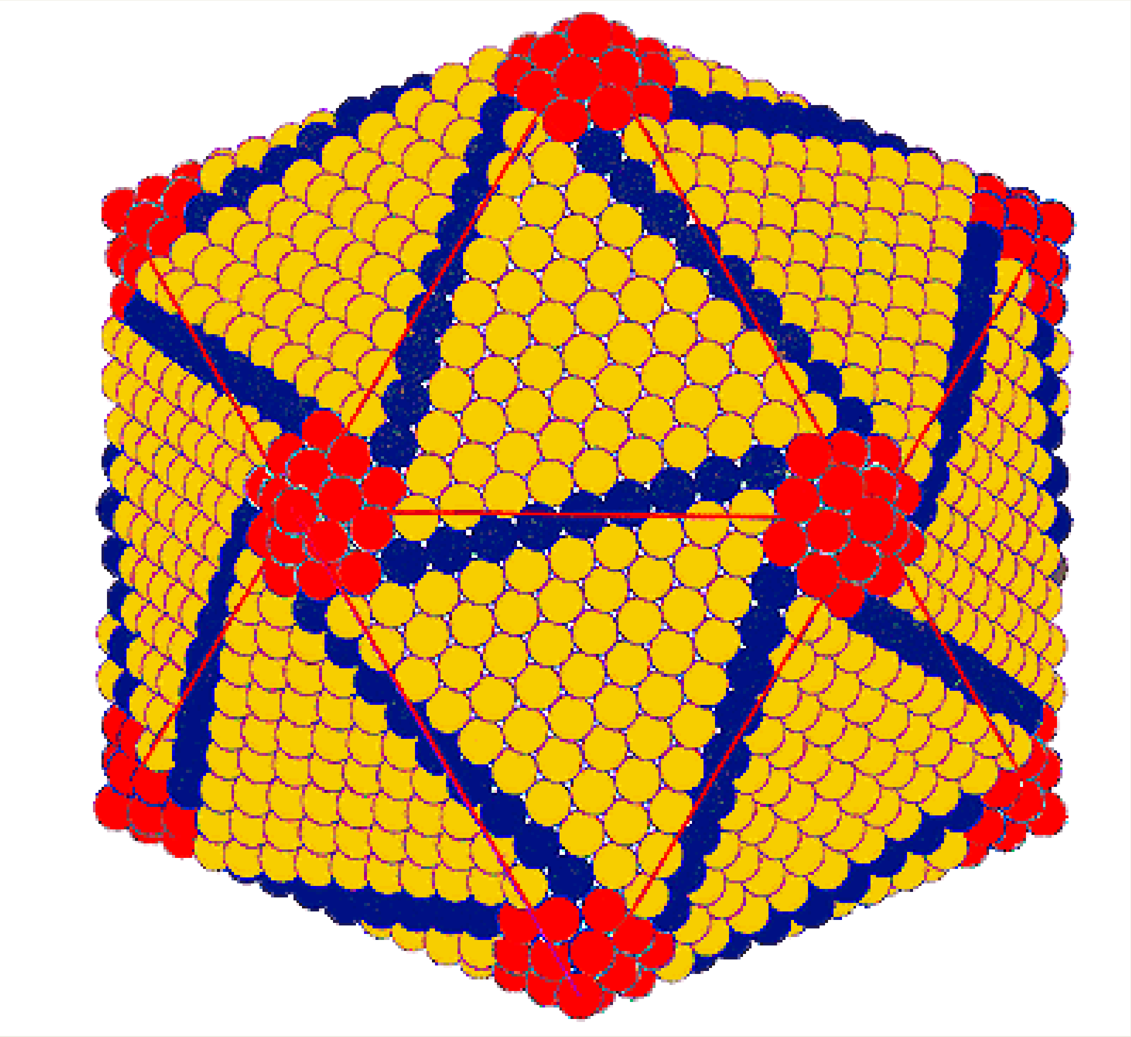


NC protein

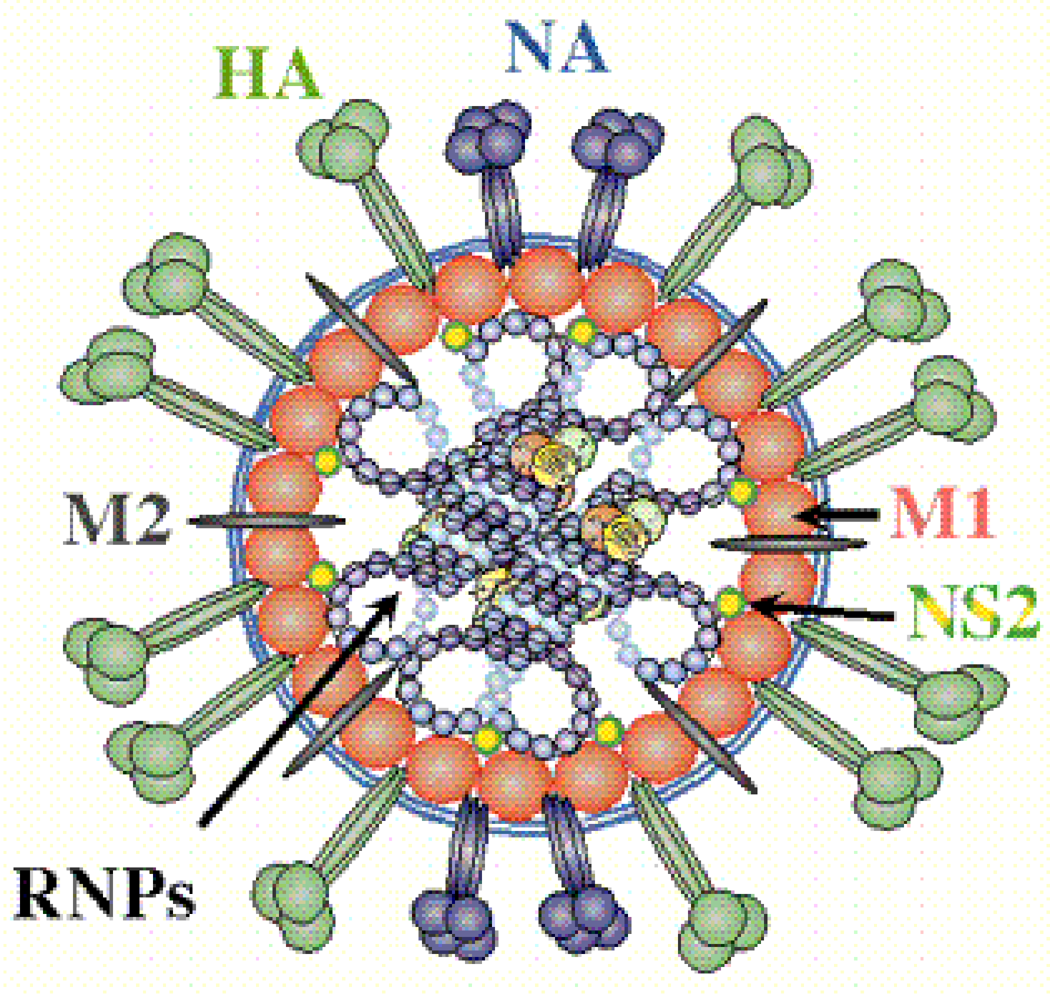
Images:P. Sforza, 2001

www.ppws.vt.edu/~sforza/tmv/tmv.html

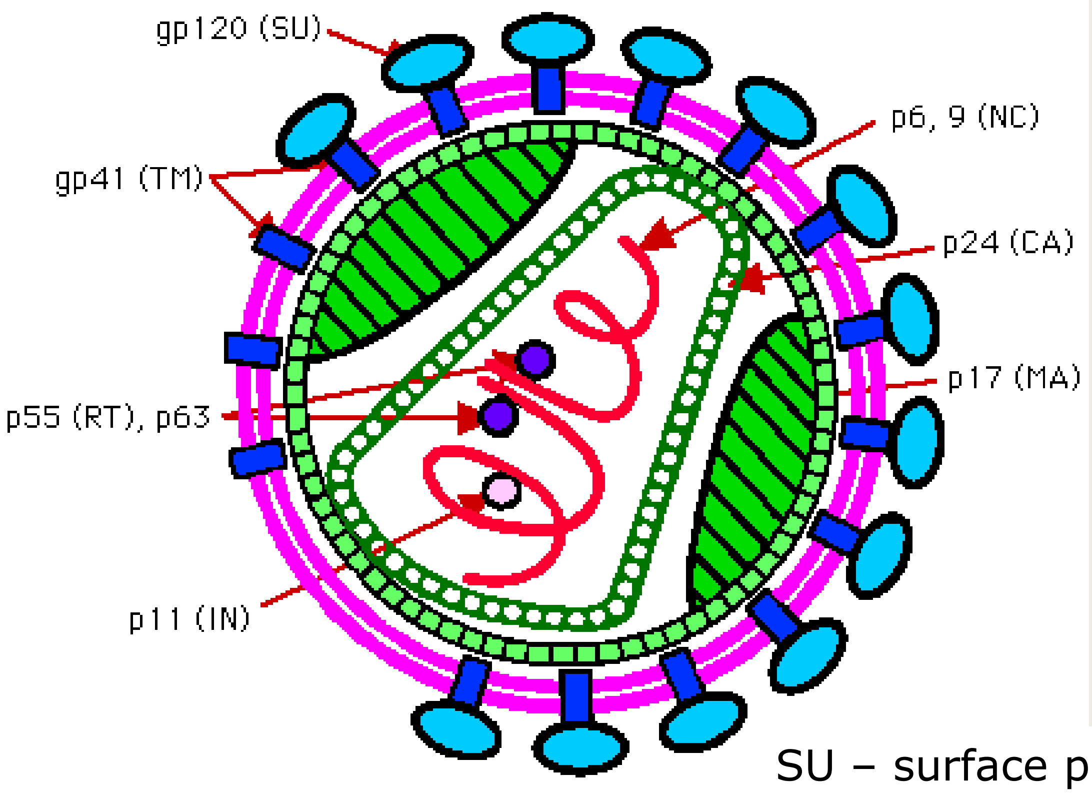
Икосаэдры: иридовирусы



Orthomyxoviruses: общая структура



- **haemagglutinin** (**HA**), a 135Å trimer
- **neuraminidase** (**NA**), a 60Å tetramer
- The inner side of the envelope is lined by the **matrix protein**.



SU – surface protein (gp120)
TM – transmembrane (gp41)
NC – nucleocapsid (p9/6)
RT – reverse transcriptase (p55)
CA – capsid protein (p24)
MA – matrix protein (p17)
IN – integrase (p11)

Вирус иммунодефицита: структура

Преимущества наличия липидной мембраны (у вирусов животных)

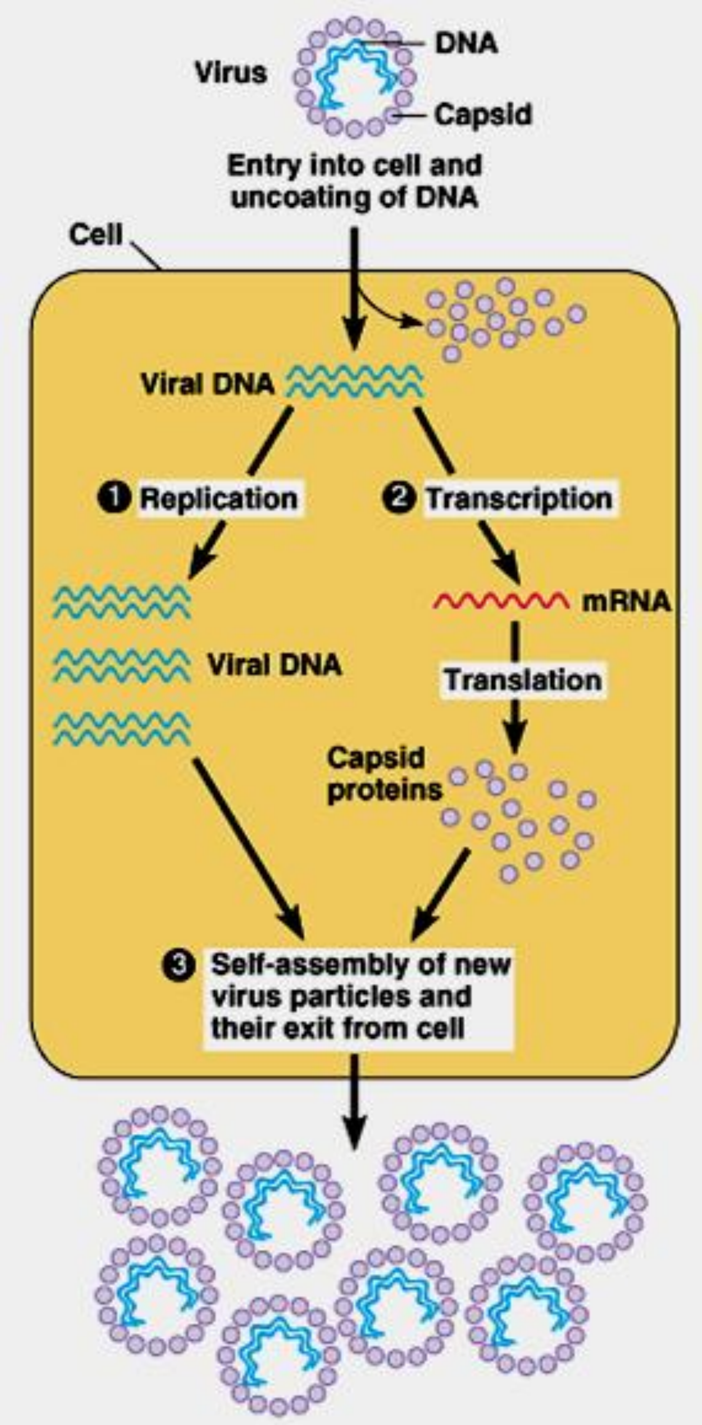
- Возможность встроить свои белки как прикрепительные и антирецепторы для точного выбора мишени
- Возможность слияния оболочки вируса и почкования без лизиса клетки-хозяина
- Снижение иммунного ответа за счет наличия хозяйских рецепторов

Стратегия размножения вирусов

1. проникнуть в клетку хозяина
2. избежать разрушения в клетке хозяина
3. заставить метаболические пути и белок-синтезирующую систему клетки хозяина работать на репликацию вирусных частиц

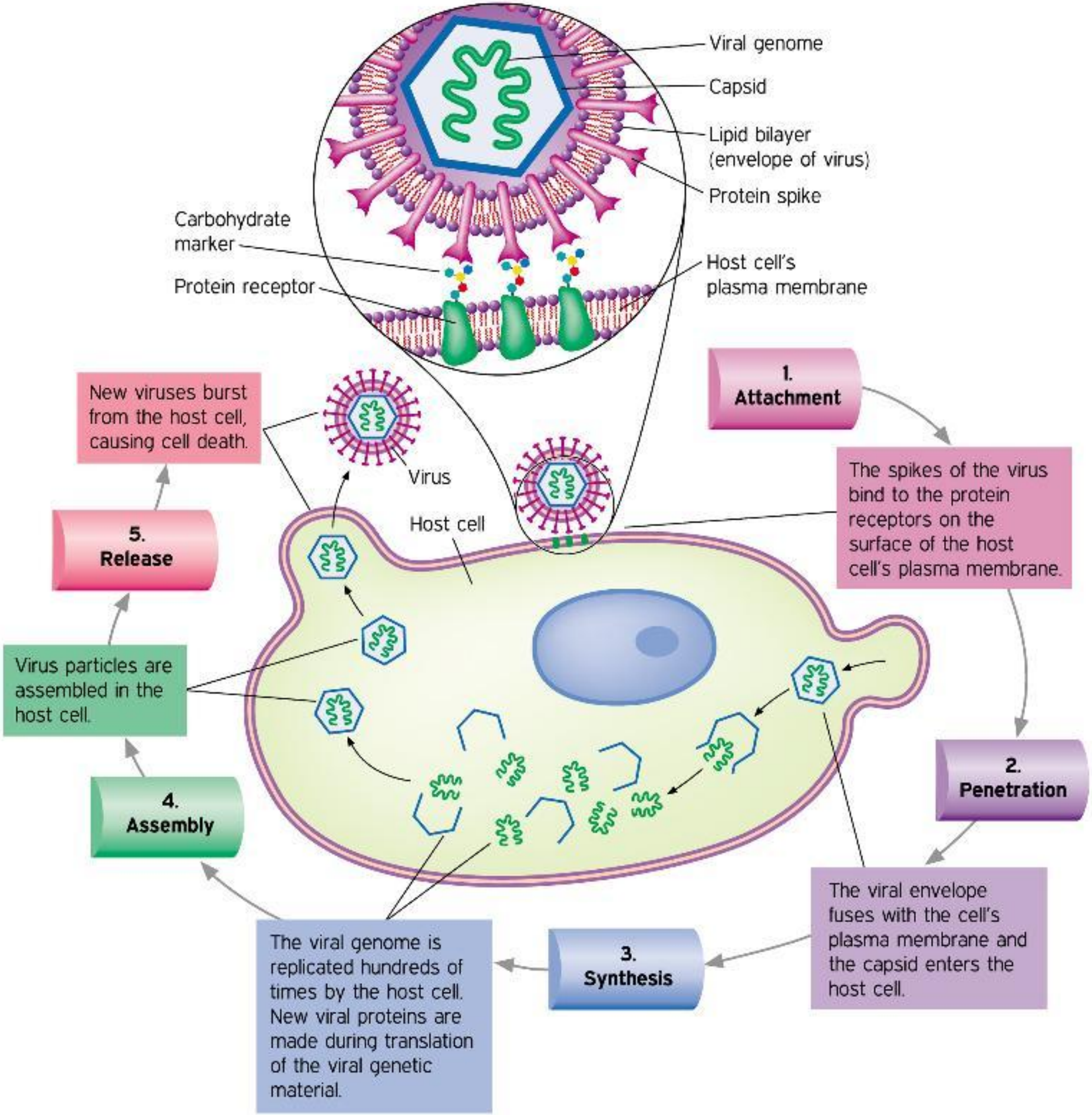
Этапы репликации

1. инициация (инфицирование клетки)
2. репликация (копирование генома вируса, белков капсида и сборка вирусных частиц)
3. высвобождение зрелых вирионов


Virus
DNA
Capsid
Entry into cell and uncoating of DNA
Cell
Viral DNA
❶ Replication
❷ Transcription
mRNA
Viral DNA
Translation
Capsid proteins
❸ Self-assembly of new virus particles and their exit from cell

Mechanisms of Viral Pathogenesis

- Binding to host cells and invasion
  - All viruses **have surface proteins** to interact with specific host cell receptors
  - Once attached, viruses are taken up through receptor mediated **endocytosis** or membrane fusion
    - Membrane fusion occurs in enveloped viruses
  - Viruses released from infected cell may infect new cell or disseminate into bloodstream



1. Attachment

The spikes of the virus bind to the protein receptors on the surface of the host cell's plasma membrane.

2. Penetration

The viral envelope fuses with the cell's plasma membrane and the capsid enters the host cell.

3. Synthesis

The viral genome is replicated hundreds of times by the host cell. New viral proteins are made during translation of the viral genetic material.

4. Assembly

Virus particles are assembled in the host cell.

5. Release

New viruses burst from the host cell, causing cell death.

Варианты транскрипционных программ вирусов

- ДНК-содержащие
- РНК-содержащие (позитивный геном или негативный геном)

Варианты развития: литический цикл и лизогенный (отодвинутый литический) цикл

LYTIC CYCLE	**LYSOGENIC CYCLE**
the virus reproductive cycle results in the death of the host. - *Virulent phages* (like T4) reproduce only by a lytic cycle	The virus genome replicates without destroying the host cell. *Temperate phages*, like phage lambda ( ), may use both lytic and lysogenic cycles. Within the host, the virus’ circular DNA engages in either the lytic or lysogenic cycle.

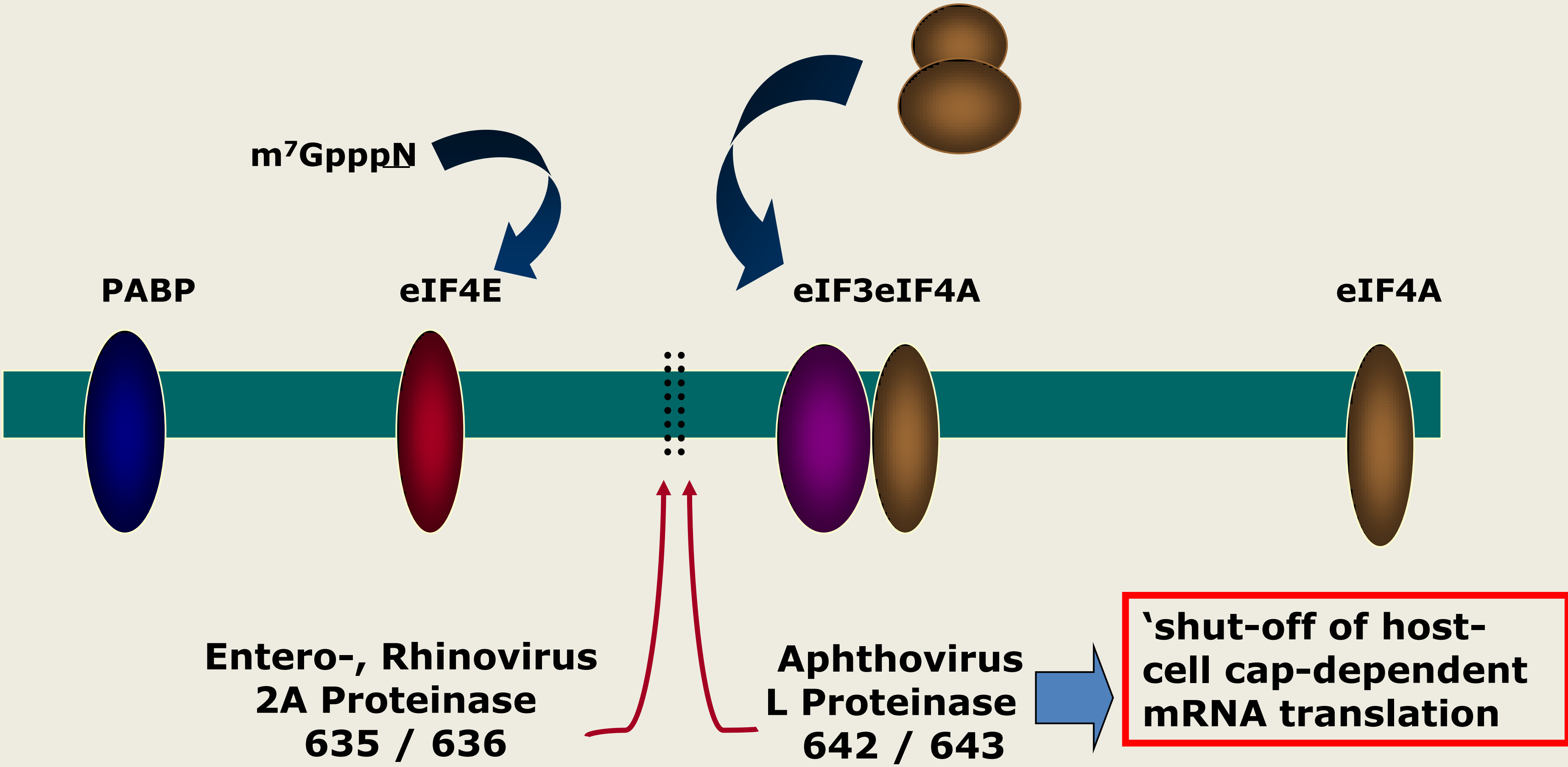
‘Reprogramming’ the cell by viruses

1) ‘Shut-off’ of host-cell translation:

-By modification of translation factors
-By miRNA (interference)
-By modulation of mRNA nuclear export

2) Remodeling of cell structure (cytoskeleton, membranes) and metabolism

Stop of Eukaryotic translation by viruses



Entero-, Rhinovirus
2A Proteinase
635 / 636

Aphthovirus
L Proteinase
642 / 643

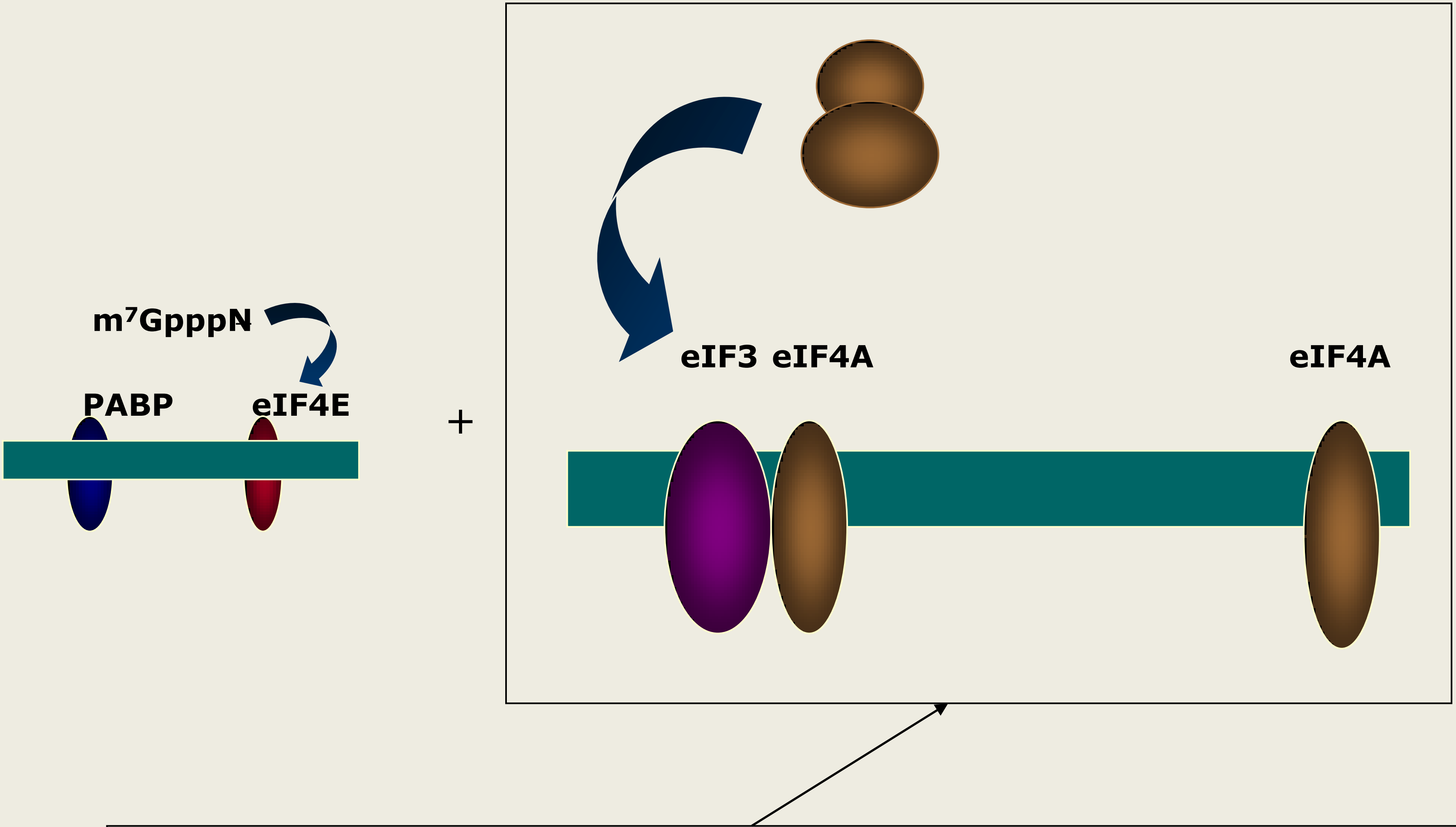
‘shut-off of host-cell cap-dependent mRNA translation

eIF4E - cap binding

eIF4A - bidirectional RNA helicase

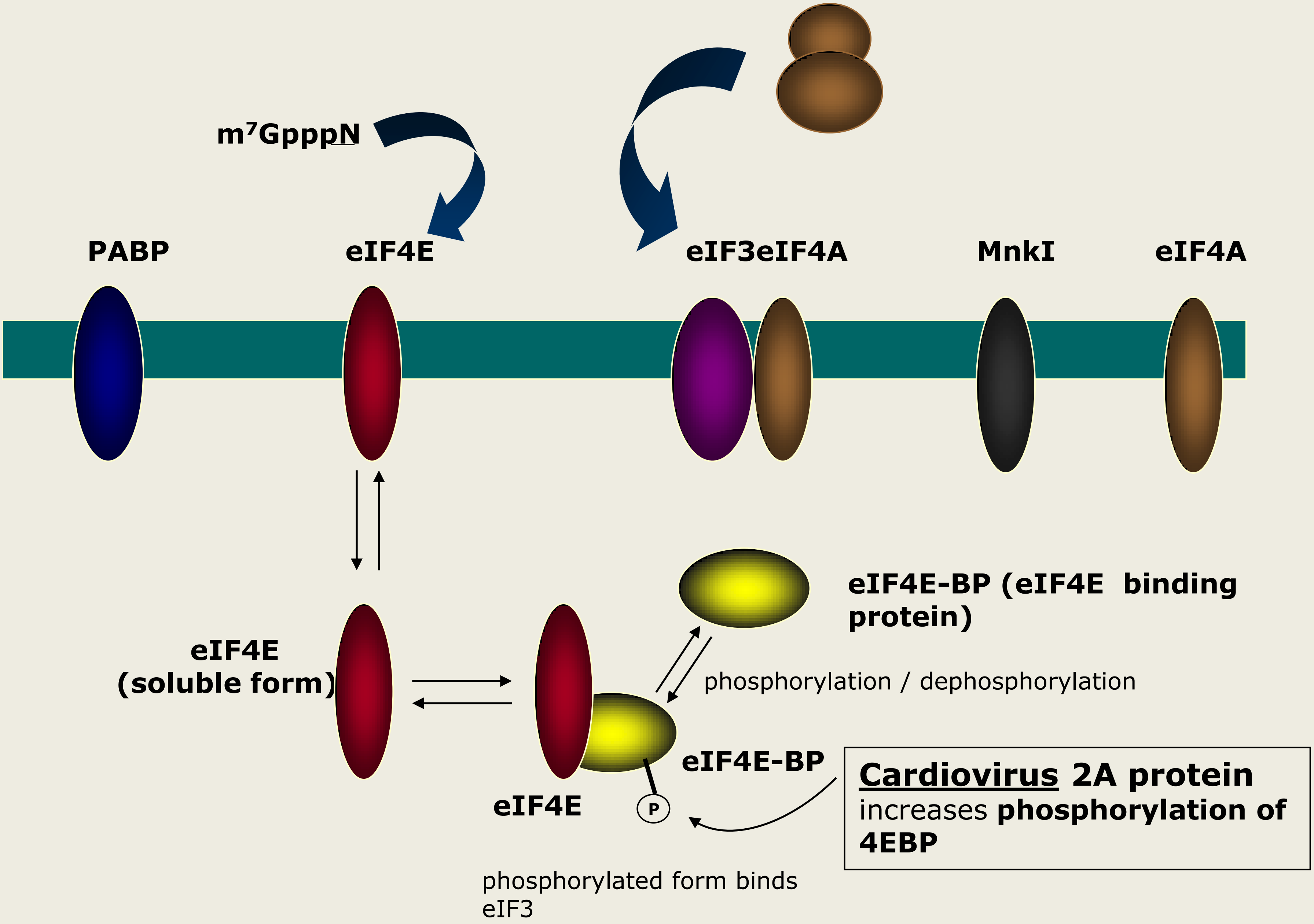
eIF3 - ribosome binding

PABP – poly(A) binding protein



the internal ribosome entry segment (IRES)can bind **this portion of the (cleaved) initiation complex directly to initiate virus translation**

Eukaryotic Initiation Factor 4G (eIF4G)



m^7GpppN

PABP

eIF4E

eIF3eIF4A

MnkI

eIF4A

eIF4E (soluble form)

eIF4E-BP (eIF4E binding protein)

phosphorylation / dephosphorylation

eIF4E-BP

eIF4E

P

phosphorylated form binds eIF3

Cardiovirus 2A protein increases **phosphorylation of 4EBP**

Стратегия защиты хозяина от вирусной НК

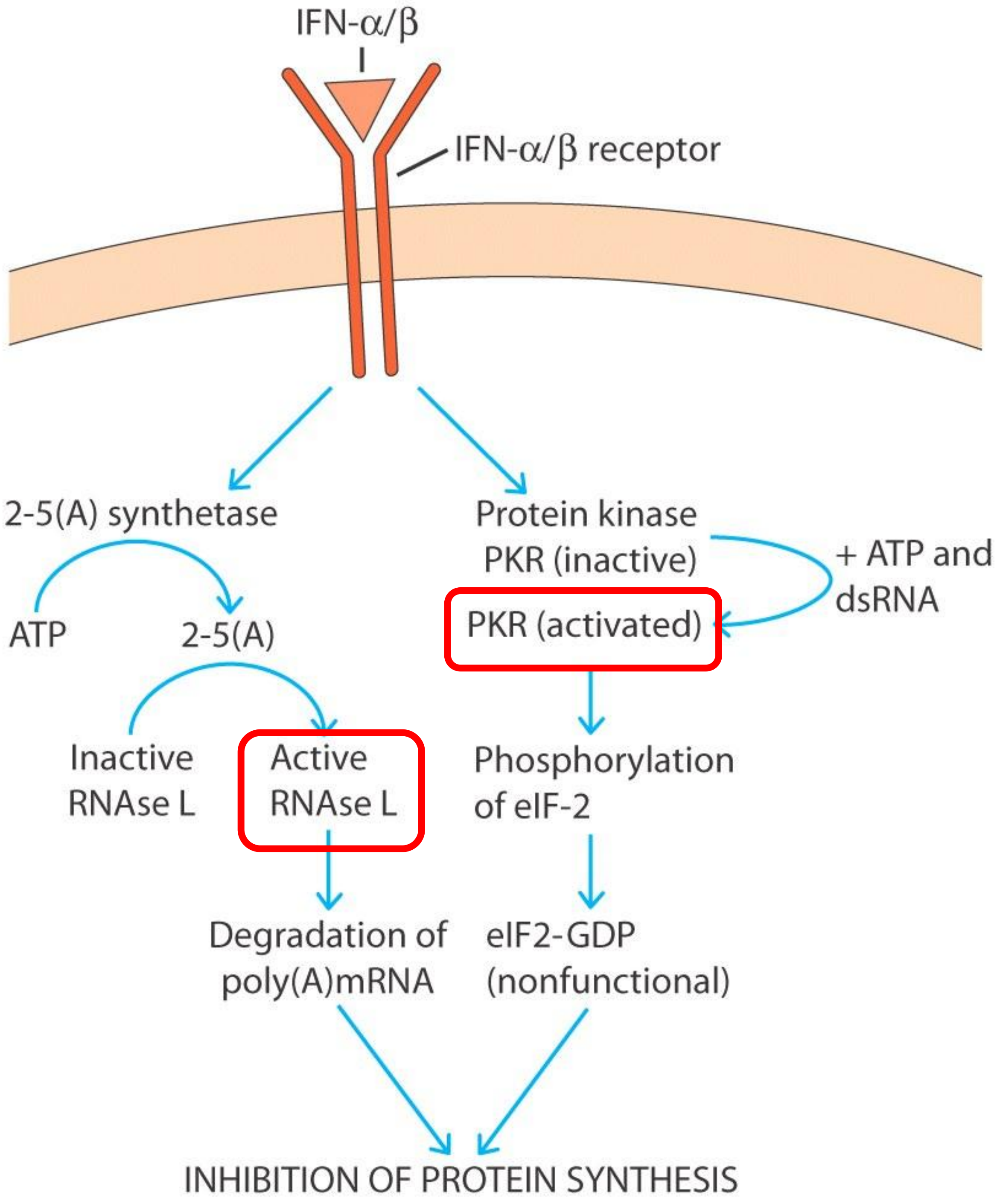
- Полиаденилатсинтетаза синтезирует полиаденилаты 2’-5’ из АТФ, активация **РНК-азы L для деградации всей РНК** (и клеточной и вирусной)
- Активируется **протеинкиназа R**, фосфорилирование фактора инициации eIF2, **полная блокада трансляции**

Viral Evasion of Host

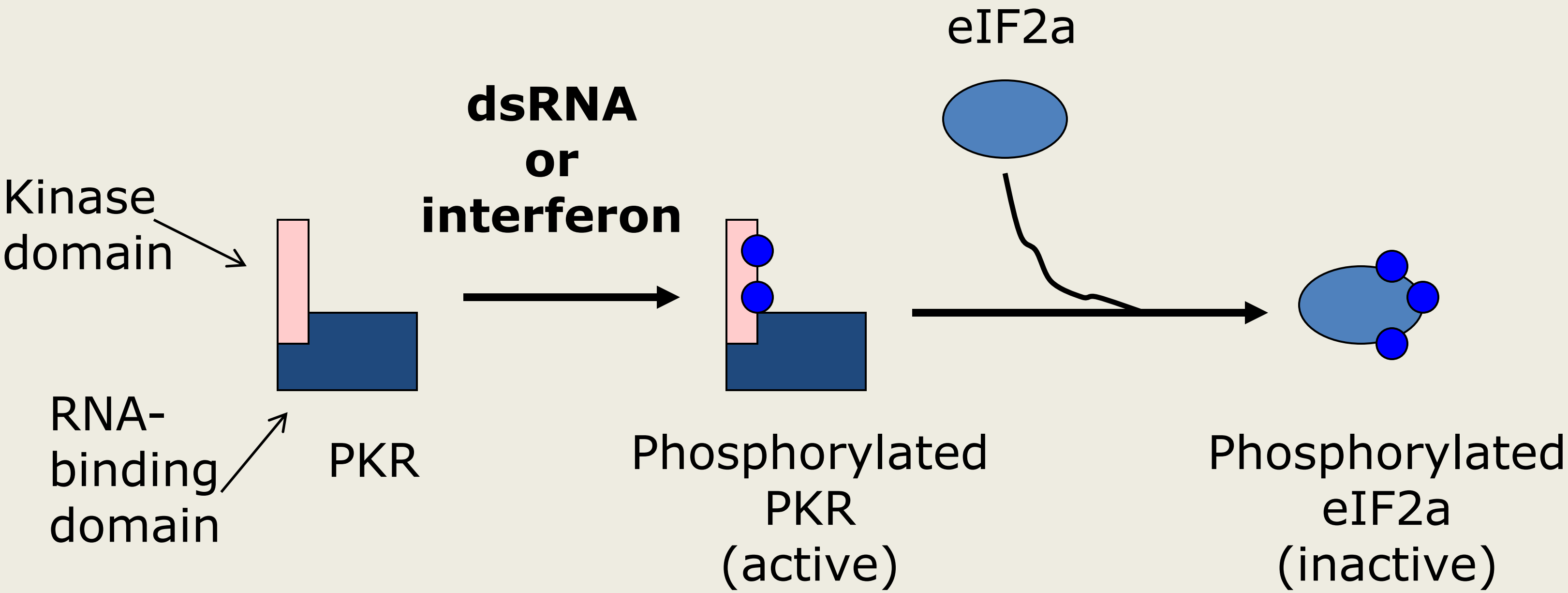
- **interferons** play a role in limiting the ability of viruses moving from neighbor cell to neighbor cell
  - once infected cells are capable of producing a protein that can regulate and limit viral replication
    - some viruses are able to encode proteins to shut down this cellular protective device

Cells can avoid being hijacked by viruses by activating the Protein Kinase R (PKR) pathway. PKR is **triggered by dsRNA and interferon**.

Shuts down protein synthesis machinery of cells, thus preventing viral replication.



Protein Kinase R: Interfering with Infection



Ответ вирусов

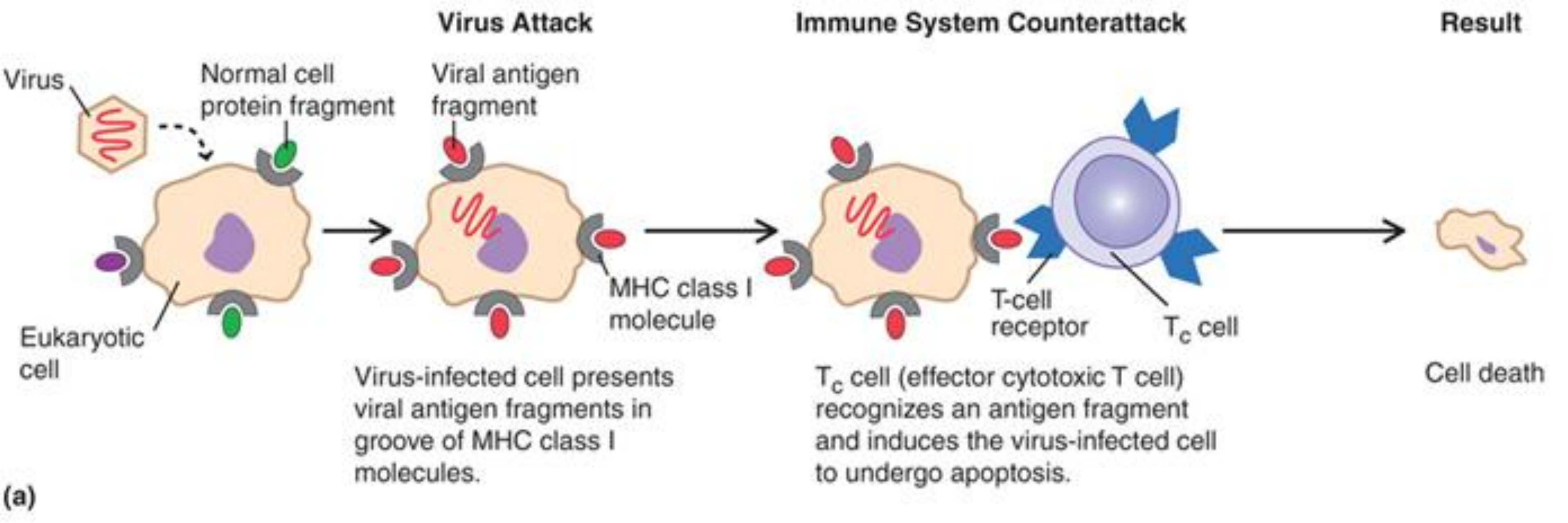
- Ингибирование PKR (через суицидный псевдосубстрат или ингибиторы, или синтез протеаз, или индукция синтеза клеточного репрессора)

Mechanisms of Viral Pathogenesis

- Avoiding immune responses
  - Avoiding antiviral effects of interferon
    - Interferons alter regulatory responses of cell in event of viral infection
      - Helps limit viral replication
        - Some viruses **encode specific proteins to interrupt inhibition of viral replication**
  - Regulation of host cell death by viruses
    - Kill host after production of large numbers of viral copies
      - Allows spread to other cells
    - Viruses prevent apoptosis
      - Inhibits protein that regulates apoptosis
    - Block antigen presentation of MHC class I
      - No sign of infection
    - Cause production of “counterfit” MHC class I molecules
      - All appears “well”

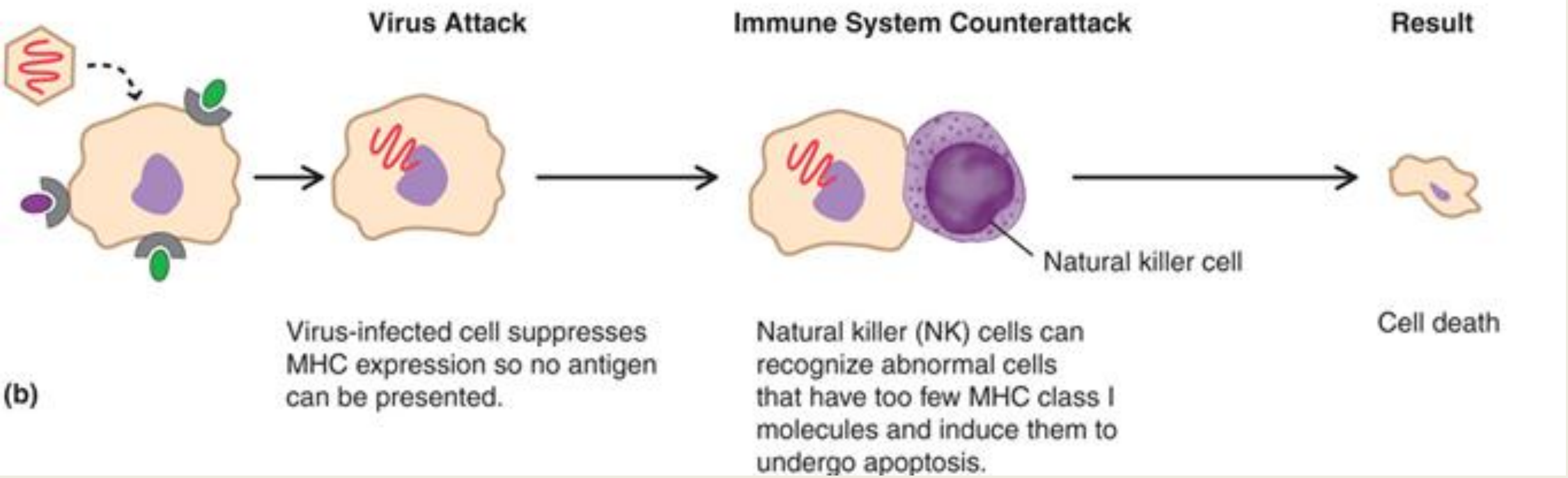
Mechanisms of Viral Pathogenesis

- Avoiding immune responses
  - Antibodies and viruses
    - Antibodies interact with extracellular viruses only
      - To avoid antibody exposure some viruses develop mechanisms to directly transfer from one cell to immediate neighbor
    - Viruses can remain intracellular by forcing neighboring cells to fuse in the formation of syncytium
    - Viruses can modify viral surface antigens
      - Viruses replicate and change faster than the human body can replicate antibody



Virus-infected cell presents viral antigen fragments in groove of MHC class I molecules.

T_c cell (effector cytotoxic T cell) recognizes an antigen fragment and induces the virus-infected cell to undergo apoptosis.

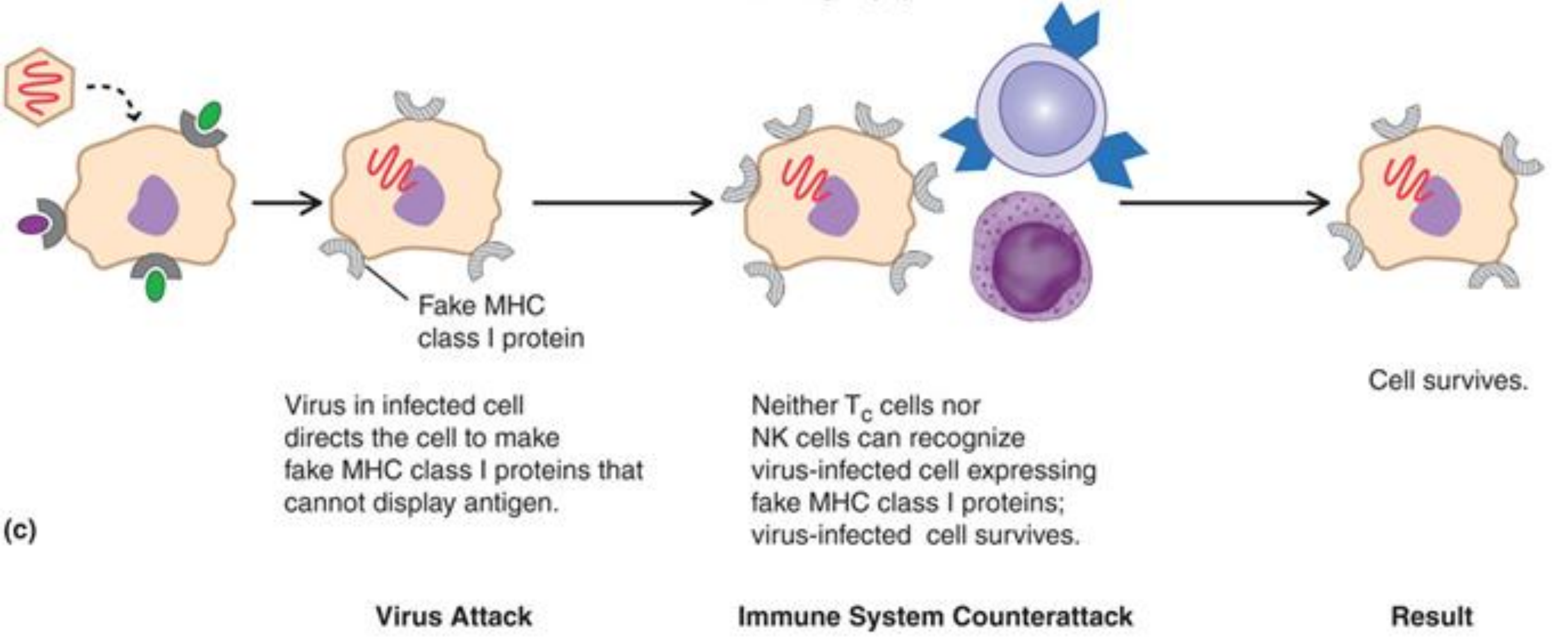


(b)

Virus-infected cell suppresses MHC expression so no antigen can be presented.

Natural killer (NK) cells can recognize abnormal cells that have too few MHC class I molecules and induce them to undergo apoptosis.

Cell death



(c)

Virus in infected cell directs the cell to make fake MHC class I proteins that cannot display antigen.

Neither T_c cells nor NK cells can recognize virus-infected cell expressing fake MHC class I proteins; virus-infected cell survives.

Cell survives.

Immune Response Damage

- inflammatory response can destroy tissue
  - antibody-antigen complexes formed during the immune response settle in kidneys and joints
    - activates complement, which produces damaging inflammation
- viral pathogenesis is very dependent on
  - gaining access to the host
  - evading the host's defenses
  - causing damage to or death of the host cell while continuing to reproduce themselves

Influenza Virus **NS1 Protein**.

Multifunctional protein - localized in both the cytoplasm and in the nucleus of *infected cells*.

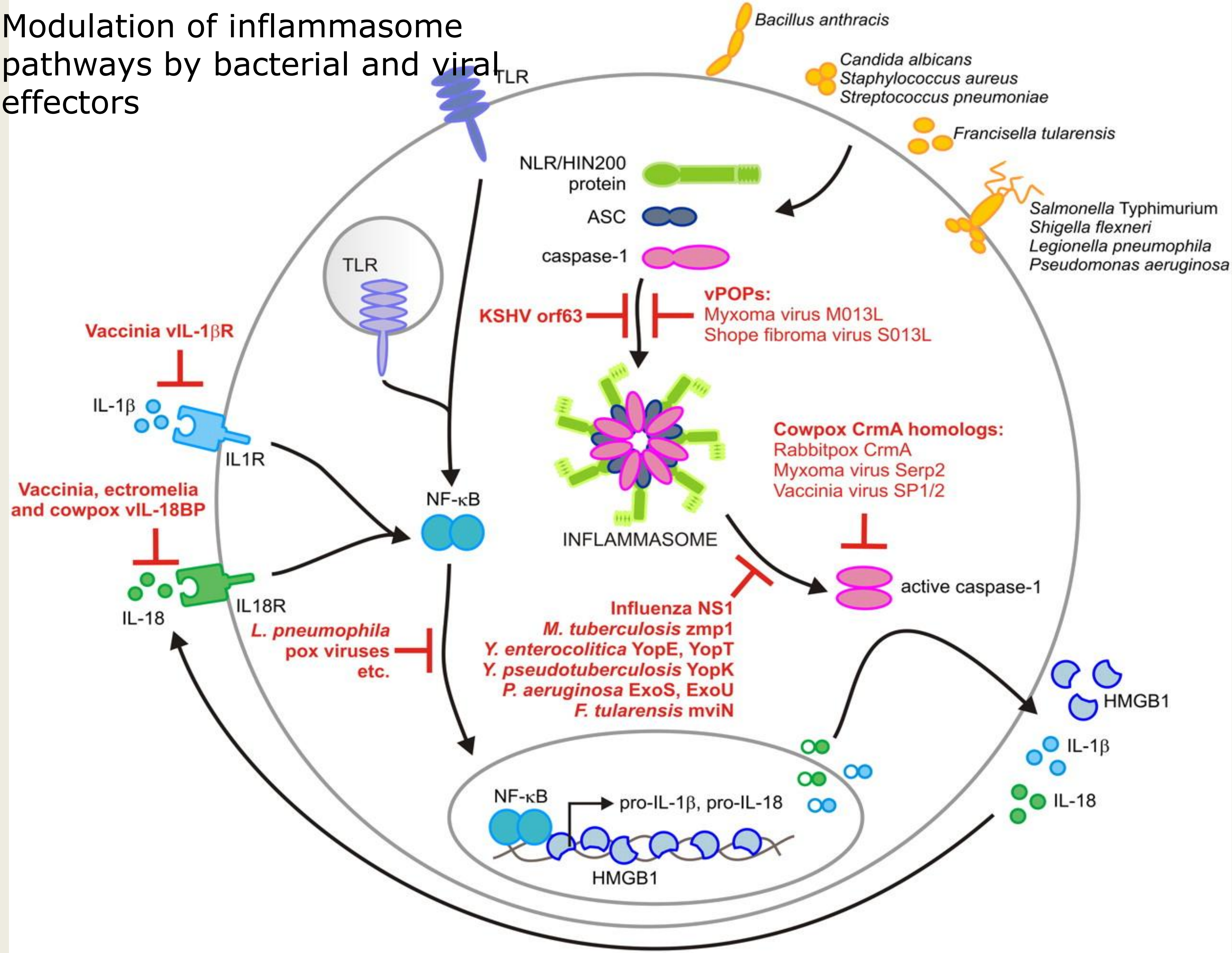
In the cytoplasm, NS1 inhibits innate immune response by forming a complex with the pathogen sensor RIG-I and by targeting PKR and the RNase L pathway.

In addition, NS1 has been shown **to activate phosphatidylinositol-3-kinase signalling, which may be important for promoting viral replication.**

In the nucleus, **NS1 inhibits host gene expression**: this effect includes mRNA processing, which is mediated by interaction of NS1 with polyadenylation factors - cleavage and polyadenylation specificity factor (CPSF) and poly(A) binding protein II (PABII) and a putative splicing factor (NS1-BP).

The binding of NS1 to CPSF and PABII inhibits polyadenylation of host mRNAs, contributing to nuclear retention of these messages.

Modulation of inflammasome pathways by bacterial and viral effectors



Viral and bacterial pathogens have evolved a number of mechanisms (shown in red) *to interfere with inflammasome assembly and activity*.

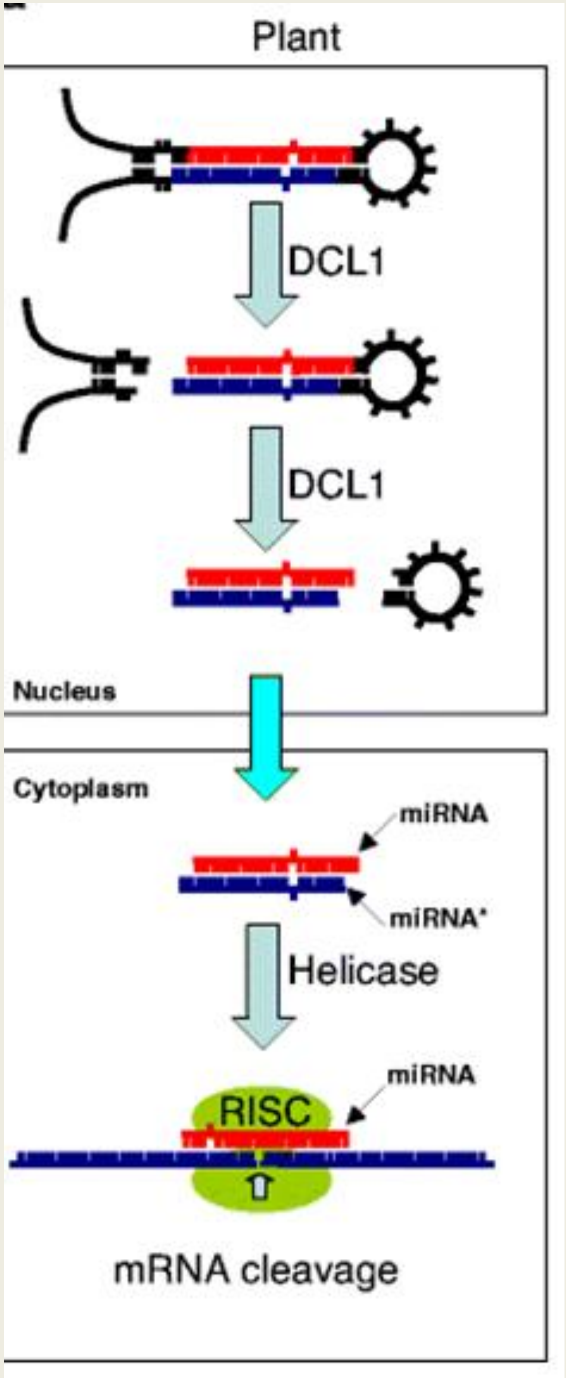
- **Inhibition of NF-κB translocation and transactivation** may result in defective synthesis of Nlrp3 and the inflammasome substrates IL-1β and IL-18.
- Orthopoxvirus pyrin-only decoy proteins (vPOPs**) scavenge the inflammasome adaptor ASC to prevent caspase-1 recruitment**. Similarly, KSHV Orf63 encodes a viral Nlrp1 decoy protein that interacts with human Nlrp1 and Nlrp3 to prevent assembly of their respective inflammasomes.
- Viruses also **target the enzymatic activity of caspase-1 directly with serpins** such as CrmA and homologous protein produced by myxoma and vaccinia virus.
- Finally, they interfere with downstream activation of IL-1β and IL-18 receptors through scavenger receptors for secreted IL-1β (vIL-1βR) and IL-18. The N-terminal RNA-binding domain of influenza virus NS1 protein inhibits caspase-1 activation and secretion of IL-1β and IL-18 through an unknown mechanism.

Стратегия защиты хозяина от вирусной НК

- Деградация РНК и блокада трансляции через фосфорилирование и работу РНКаз
- **Деградация РНК через РНК-интерференцию**

RNA-interference: virus←→host

Post-Transcriptional Gene Silencing (PTGS)



- Also called RNA interference or RNAi
- Process results in down-regulation of a gene at the RNA level (i.e., after transcription)
- *There is also gene silencing at the transcriptional level (TGS) / Examples: transposons, retroviral genes, heterochromatin*
- First discovered in plants (R. Jorgensen, 1990)
- Introduction of a transgene homologous to an endogenous gene resulted in both genes being suppressed/ also called Co-suppression
- involved enhanced degradation of the endogenous and transgene mRNAs

	Plants	Animals
# of **miRNA genes**:	100-200	100-500
Location in genome:	intergenic regions	Intergenic regions, introns
Clusters of miRNAs:	Uncommon	Common
MiRNA biosynthesis:	*Dicer*-like	*Drosha*, *Dicer*
Mechanism of repression	mRNA cleavage	Translational repression
Location of miRNA target in a gene:	Predominantly the open-reading frame	Predominantly the 3′-UTR
# of miRNA binding sites in a target gene:	Generally one	Generally multiple
Functions of known target genes:	Regulatory genes crucial for development, enzymes	Regulatory genes—crucial for development, structural proteins, enzymes

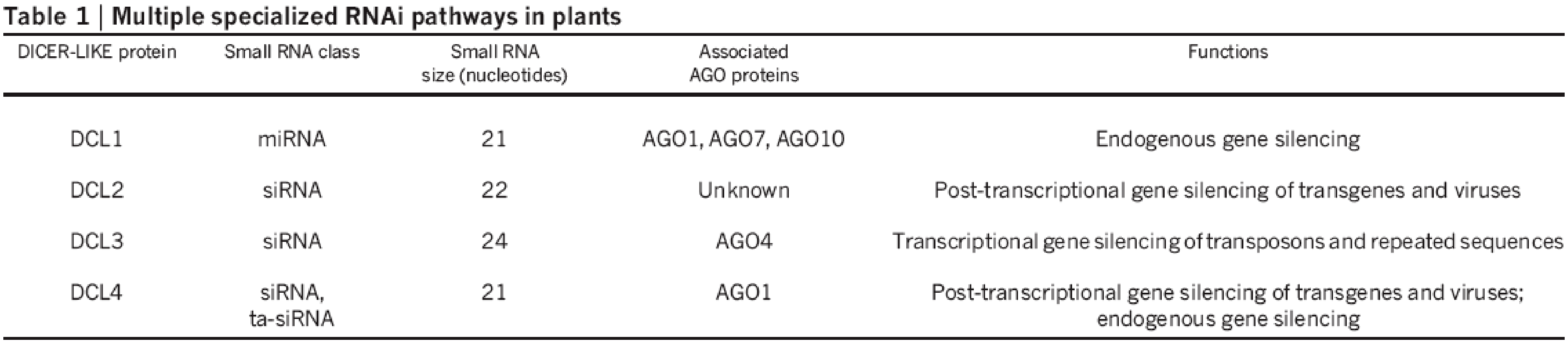


Table 1 | Multiple specialized RNAi pathways in plants

DICER-LIKE protein	Small RNA class	Small RNA size (nucleotides)	Associated AGO proteins	Functions
DCL1	miRNA	21	AGO1, AGO7, AGO10	Endogenous gene silencing
DCL2	siRNA	22	Unknown	Post-transcriptional gene silencing of transgenes and viruses
DCL3	siRNA	24	AGO4	Transcriptional gene silencing of transposons and repeated sequences
DCL4	siRNA, ta-siRNA	21	AGO1	Post-transcriptional gene silencing of transgenes and viruses; endogenous gene silencing

All three Herpesvirus subfamilies have been found to encode miRNAs

miRNA-producing DNA viruses

γ-herpesvirus

Epstein Barr virus (EBV)	23 miRNAs
Kaposi's sarcoma-associated herpesvirus (KSHV)	12 miRNAs

β-herpesvirus

Human cytomegalovirus (HCMV)	11 miRNAs

α-herpesvirus

Herpes simplex virus 1 (HSV-1)	6 miRNAs

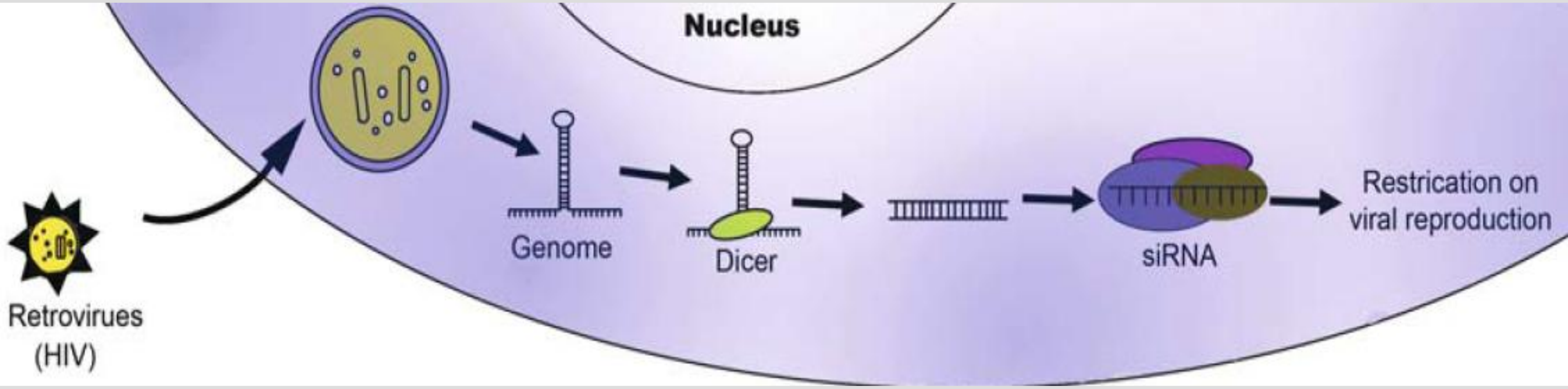
Adeno/polioma viruses	1-2 miRNAs

RNA viruses have been reported to lack miRNAs

The controversy of HIV

The HIV transactivating response (TAR) transcript has secondary structure features that suggesting that it may act as a pre-miRNA

Another miRNA derived from the HIV-1 *nef* gene



VALIDATED TARGETS OF VIRAL miRNAs

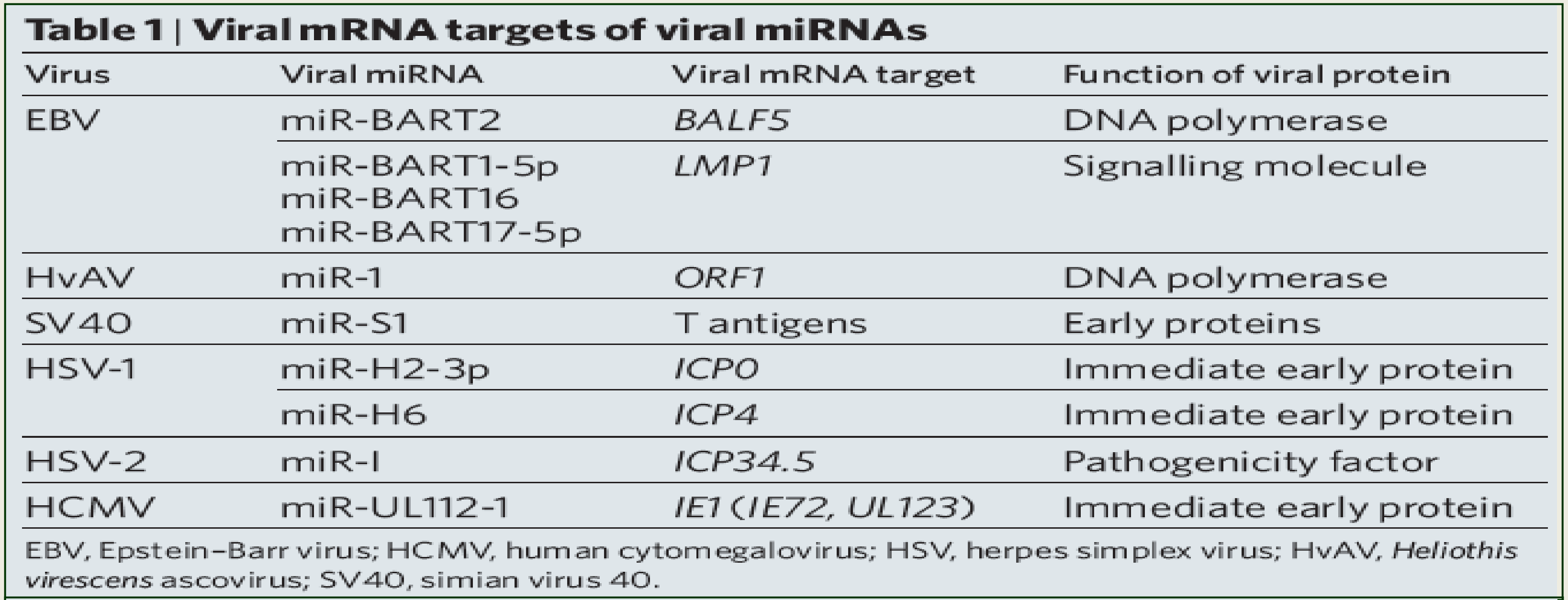


Table 1 | Viral mRNA targets of viral miRNAs

Virus	Viral miRNA	Viral mRNA target	Function of viral protein
EBV	miR-BART2	*BALF5*	DNA polymerase
	miR-BART1-5p miR-BART16 miR-BART17-5p	*LMP1*	Signalling molecule
HvAV	miR-1	*ORF1*	DNA polymerase
SV40	miR-S1	T antigens	Early proteins
HSV-1	miR-H2-3p	*ICP0*	Immediate early protein
	miR-H6	*ICP4*	Immediate early protein
HSV-2	miR-I	*ICP34.5*	Pathogenicity factor
HCMV	miR-UL112-1	*IE1* (*IE72, UL123*)	Immediate early protein

EBV, Epstein–Barr virus; HCMV, human cytomegalovirus; HSV, herpes simplex virus; HvAV, *Heliothis virescens* ascovirus; SV40, simian virus 40.

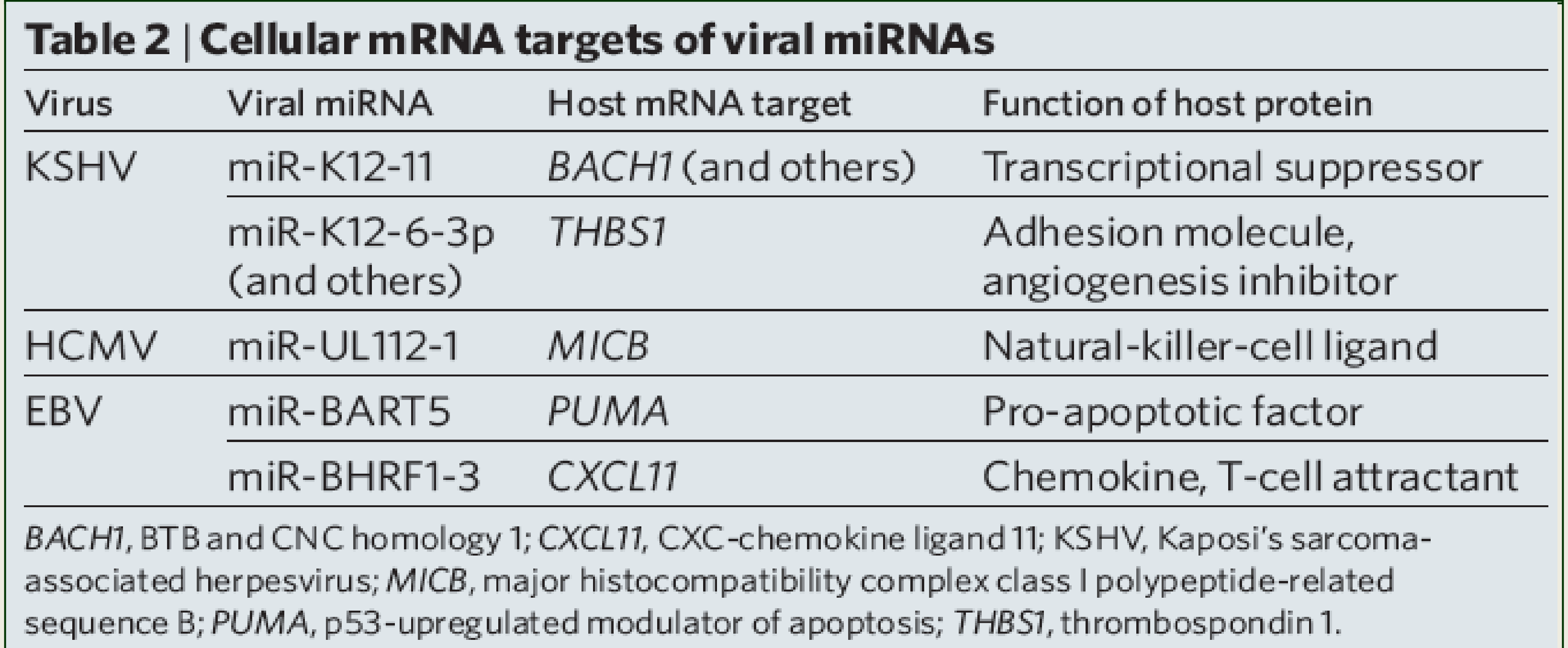


Table 2 | Cellular mRNA targets of viral miRNAs

Virus	Viral miRNA	Host mRNA target	Function of host protein
KSHV	miR-K12-11	*BACH1* (and others)	Transcriptional suppressor
	miR-K12-6-3p (and others)	*THBS1*	Adhesion molecule, angiogenesis inhibitor
HCMV	miR-UL112-1	*MICB*	Natural-killer-cell ligand
EBV	miR-BART5	*PUMA*	Pro-apoptotic factor
	miR-BHRF1-3	*CXCL11*	Chemokine, T-cell attractant

BACH1, BTB and CNC homology 1; *CXCL11*, CXC-chemokine ligand 11; KSHV, Kaposi's sarcoma-associated herpesvirus; *MICB*, major histocompatibility complex class I polypeptide-related sequence B; *PUMA*, p53-upregulated modulator of apoptosis; *THBS1*, thrombospondin 1.

VIRUS-ENCODED miRNAs AND VIRAL PATHOGENESIS

- Several **viruses** have now been shown to **reshape** the cellular environment **by reprogramming** the host's RNA-interference machinery

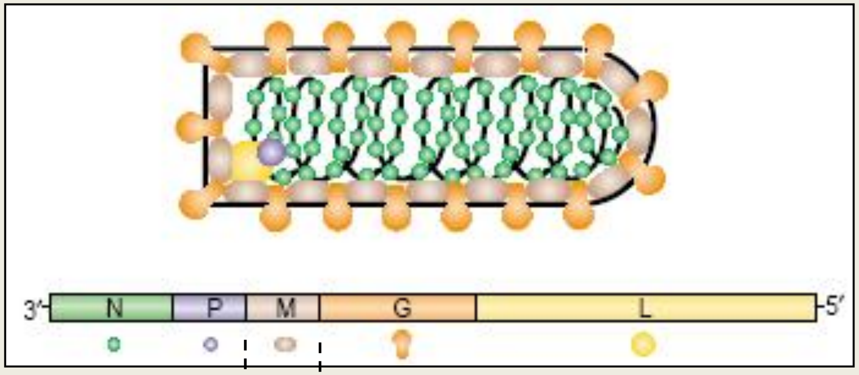
Viral microRNAs are particularly important for

- regulating the transition from latent to lytic replication and for
- attenuating antiviral immune responses

Re-modelling nuclear pores

Vesicular Stomatitis Virus (VSV) : Rhabdovirus

single-stranded,
-ve sense RNA genome,
~11kb



5 major virus proteins:

nucleoprotein (N)
phosphoprotein (P)
matrix protein (M)
glycoprotein (G)
(large) polymerase protein (L)

A defect in bulk poly(A) RNA export can be caused either by a direct disruption of the mRNA **export machinery** or by an indirect effect on mRNA biogenesis.

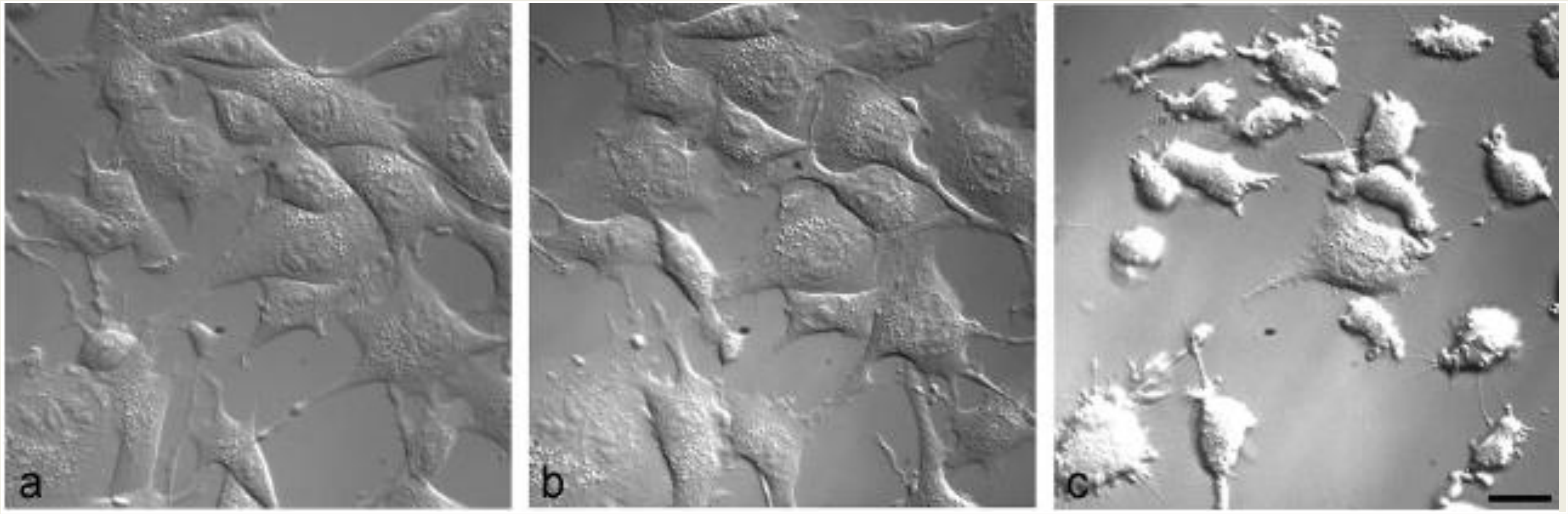
One example of interference with the mRNA export pathway is viral-host interactions involving **mRNA export factors**.

VSV M protein binds the mRNA nuclear export factor **Rae1** that is in complex with the nucleoporin **Nup98**, resulting in nuclear retention of cellular mRNAs.

(Rae1 attaches cytoplasmic mRNPs to the cytoskeleton)

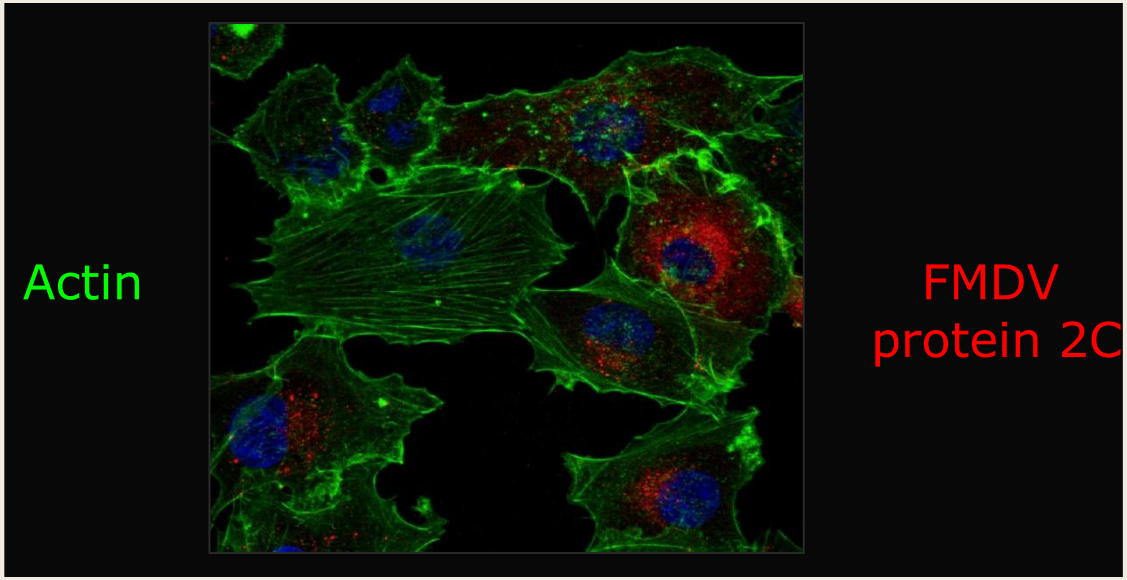
Re-modelling the Cytoskeleton

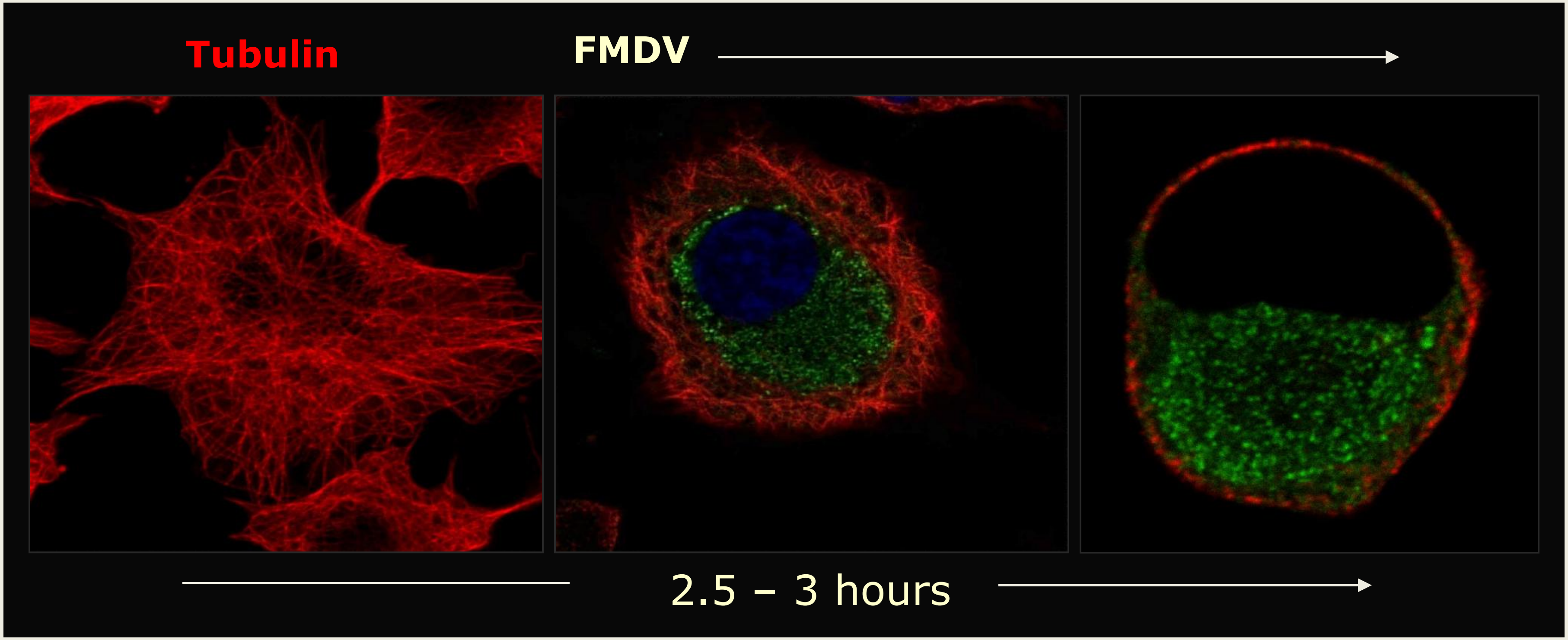
Cytopathic Effect in FMDV-infected Cells



0 hrs 1.25 hrs 2.5 hrs

Armer,H., Moffat,K., Wileman,T., Belsham,G.J., Jackson,T., Duprex,W.P., Ryan,M.D. & Monaghan, P. (2008). Foot-and-Mouth Disease Virus, but Not Bovine Enterovirus, Targets the Host Cell Cytoskeleton via the Nonstructural Protein 3C^{pro}. *J. Virol*. 82, 10556–10566.


Actin
FMDV protein 2C


Tubulin
FMDV
2.5 – 3 hours

Re-modelling the Endomembrane system

Re-modelling cytoplasmic membranes

All positive-stranded RNA viruses situate their replication complexes on membranous surfaces. Many different viruses have been shown to *induce* changes in membrane structures.

Picornaviruses: poliovirus-infected cells contain virus-induced vesicles derived from the ER.

Flaviviruses: ‘convoluted membranes’ and ‘vesicle packets’ containing cellular protein markers from the intermediate compartment (IC) and the *trans*- Golgi network (TGN).

Hepatitis C virus: A ‘membranous web’ of vesicles is formed – associated with, and derived from, the ER.

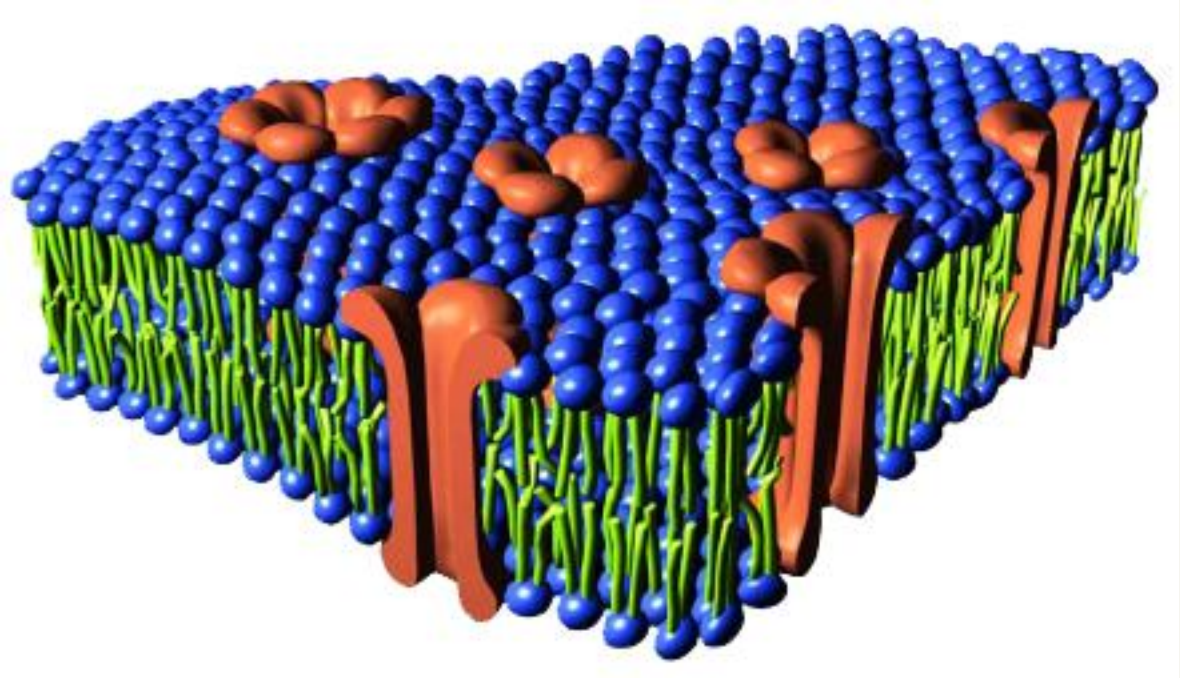
Pestiviruses: BVDV-infected cells contain tubules and vesicles derived from the rough ER.

Alphaviruses: Sindbis virus (SV) and Semliki Forest Virus (SFV)-infected cells show membrane invaginations and spherules associated with lysosome and endosomes.

Rubella: Replication complexes are situated on lysosomes.

Nodaviruses: Flock House Virus (FHV) replicates in spherules formed by invaginations of mitochondrial membranes.

Plant +ve strand RNA viruses also use the surface of vacuoles and chloroplasts



Viroporins alter membrane permeability: a physical pore is formed upon oligomerisation within membranes.

VIROPORINS

Picornaviridae	Poliovirus	2B	97aa
Togaviridae	SFV	6K	60aa
	Sindbis virus	6K	55aa
	Ross River virus	6K	62aa
Flaviviridae	HCV	p7	63aa
Retroviridae	HIV-1	Vpu	81aa
Paramyxoviridae	HRSV	SH	64aa
Orthomyxoviridae	Influenza A virus	M2	97aa
Reoviridae	ARV	p10	98aa
Phycodnaviridae	PBCV-1	Kcv	94aa
Rhabdoviridae	BEFV	alpha 10p	88aa

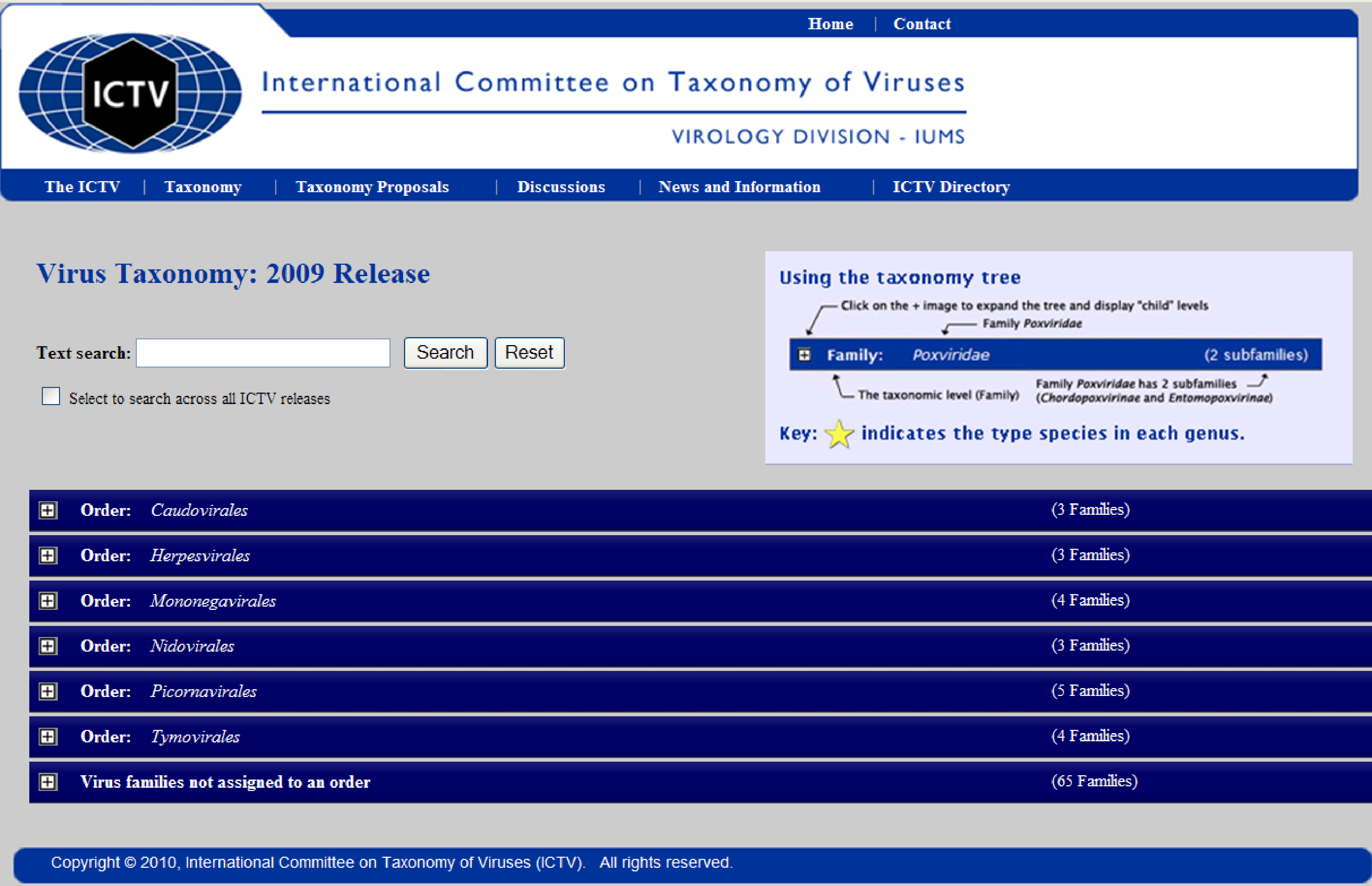
The M2 Proton Channels of Influenza A and B Viruses.

M2 proteins are homo-tetrameric, type III integral membrane proteins containing a small N-terminal ectodomain, a single transmembrane domain, and C-terminal cytoplasmic tail.

The A/M2 ion channel protein of influenza A virus is found in the virion.

The transmembrane **domain acts as a signal sequence to target the nascent polypeptide domain to the membrane of the endoplasmic reticulum as it emerges from the ribosome**, and this hydrophobic domain also serves as the stop-transfer sequence to anchor the protein in the membrane.

http://ictvonline.org/virusTaxonomy.asp?version=2011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The ICTV | Taxonomy | Taxonomy Proposals | Discussions | News and Information | ICTV Directory
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Reset

Virus Taxonomy: 2009 Release

Text search:

☐ Select to search across all ICTV releases

Using the taxonomy tree

Click on the + image to expand the tree and display "child" levels

Family *Poxviridae*

⊞ **Family:** *Poxviridae* (2 subfamilies)

The taxonomic level (Family)

Family *Poxviridae* has 2 subfamilies (*Chordopoxvirinae* and *Entomopoxvirinae*)

Key: ☆ **indicates the type species in each genus.**

⊞ **Order:** *Caudovirales* (3 Families)

⊞ **Order:** *Herpesvirales* (3 Families)

⊞ **Order:** *Mononegavirales* (4 Families)

⊞ **Order:** *Nidovirales* (3 Families)

⊞ **Order:** *Picornavirales* (5 Families)

⊞ **Order:** *Tymovirales* (4 Families)

⊞ **Virus families not assigned to an order** (65 Families)

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Классификация вирусов по типу хозяина и НК: бактериофаги

❑ Tailed bacteriophage:dsDNA

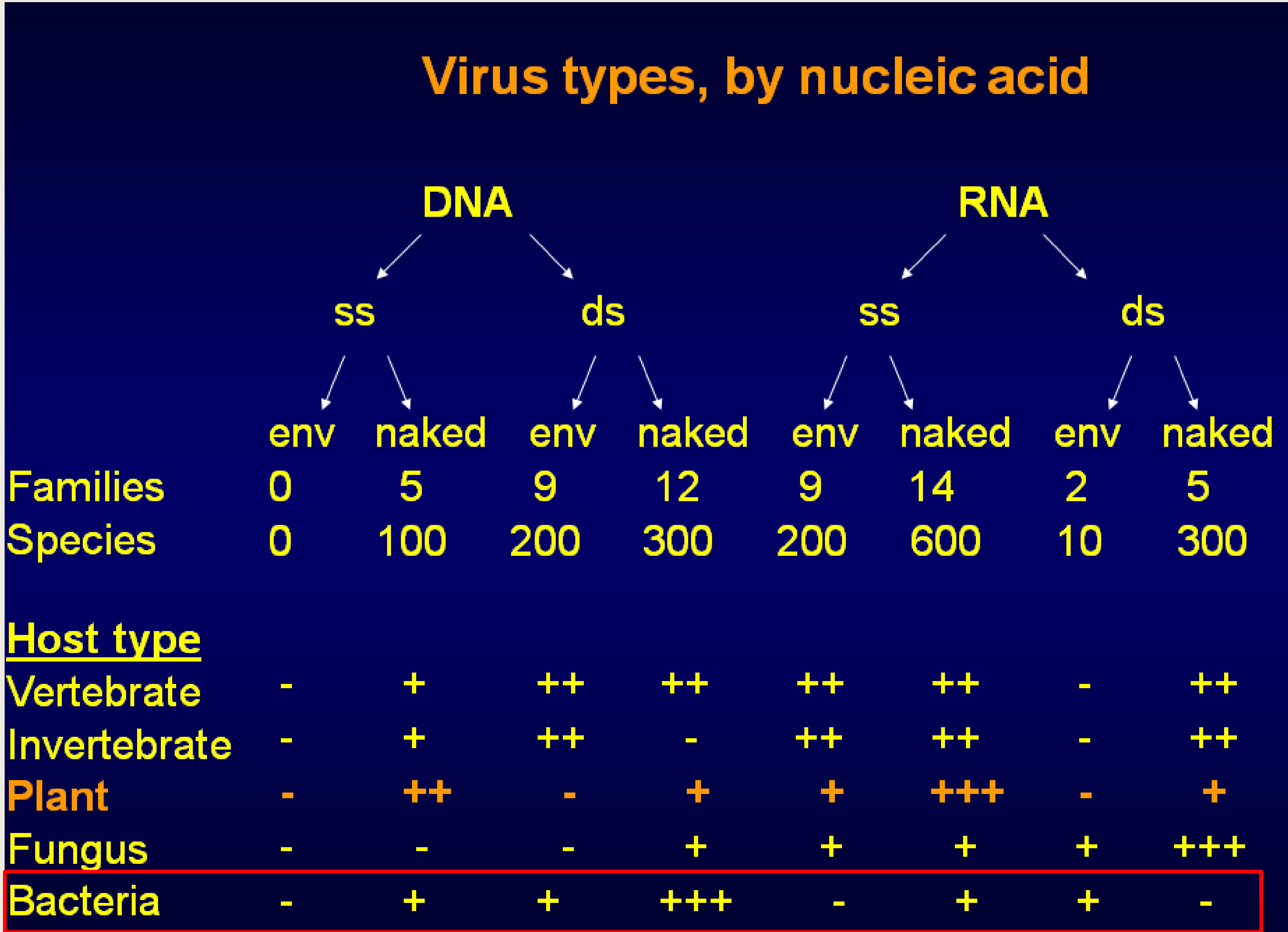
- group A (long, contractile tails -Myoviridae)
- group B (long, noncontractile tails – Styloviridae)
- group C (short tail (Pedoviridae)

❑ Cubic bacteriophage

- ss-DNA (group 1) - Microviridae (ϕX174)
- ds-DNA (group 2) - Corticoviridae (PM-2)
- ss-RNA (group 3) – Leviviridae (f2)
- ds-RNA (group 4) – Cystoviridae (ϕ6)

❑ Filamentous – Inoviridae (ssDNA; M13)

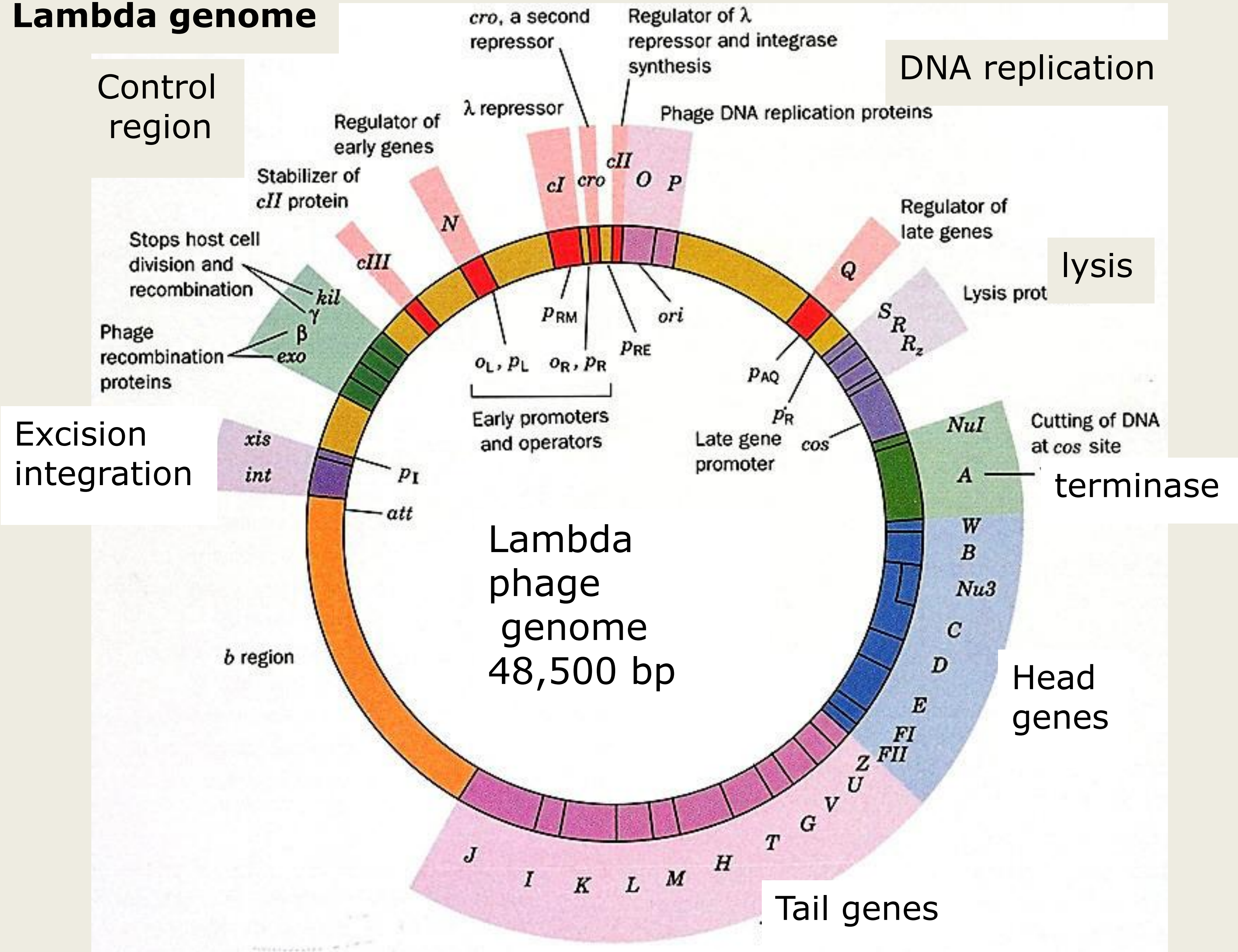
2002



Virus types, by nucleic acid

	DNA				RNA			
	ss		ds		ss		ds	
	env	naked	env	naked	env	naked	env	naked
Families	0	5	9	12	9	14	2	5
Species	0	100	200	300	200	600	10	300
Host type								
Vertebrate	-	+	++	++	++	++	-	++
Invertebrate	-	+	++	-	++	++	-	++
Plant	-	++	-	+	+	+++	-	+
Fungus	-	-	-	+	+	+	+	+++
Bacteria	-	+	+	+++	-	+	+	-

Lambda genome



Control region

DNA replication

lysis

Excision integration

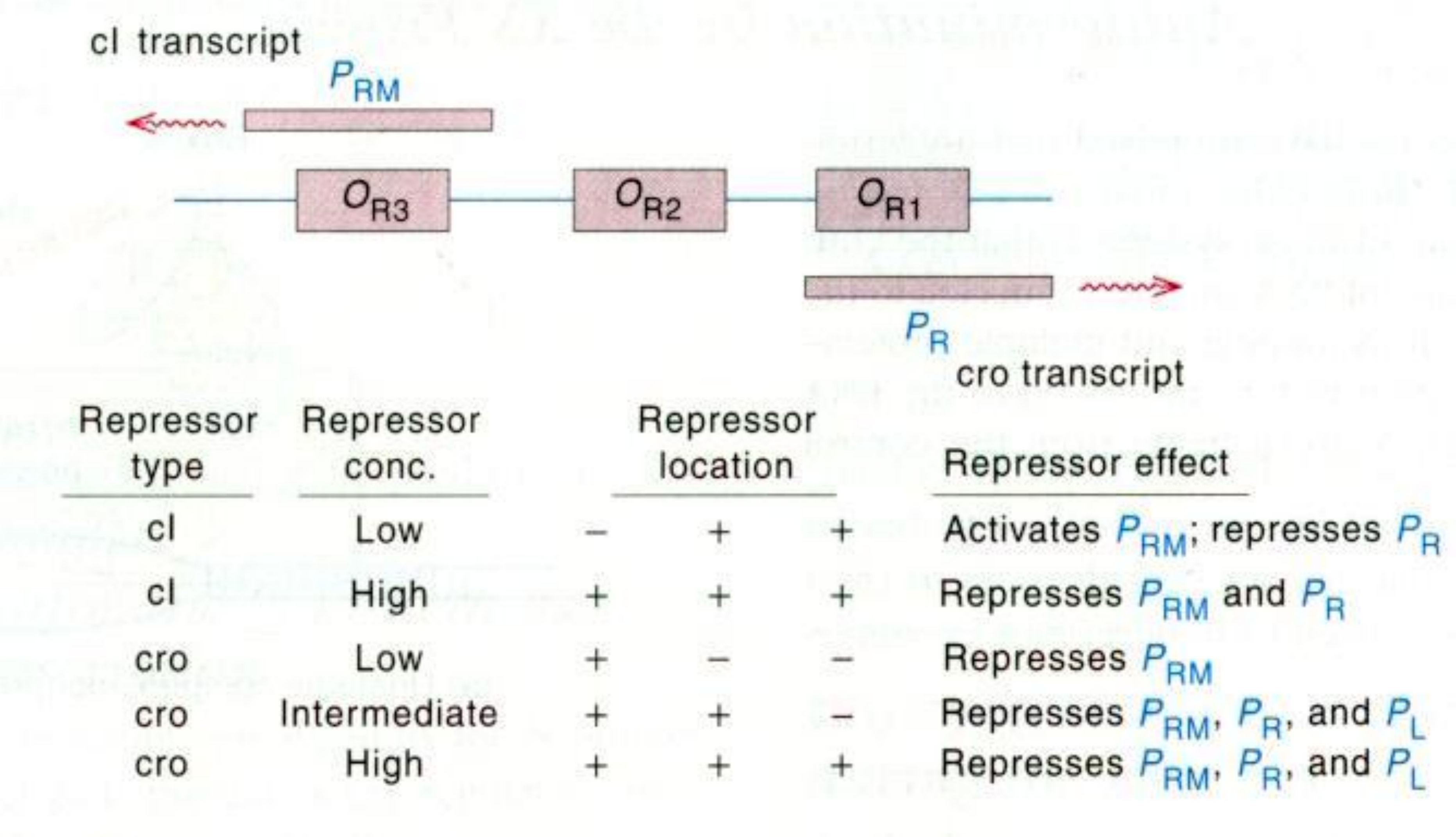
terminase

Lambda phage genome 48,500 bp

Head genes

Tail genes

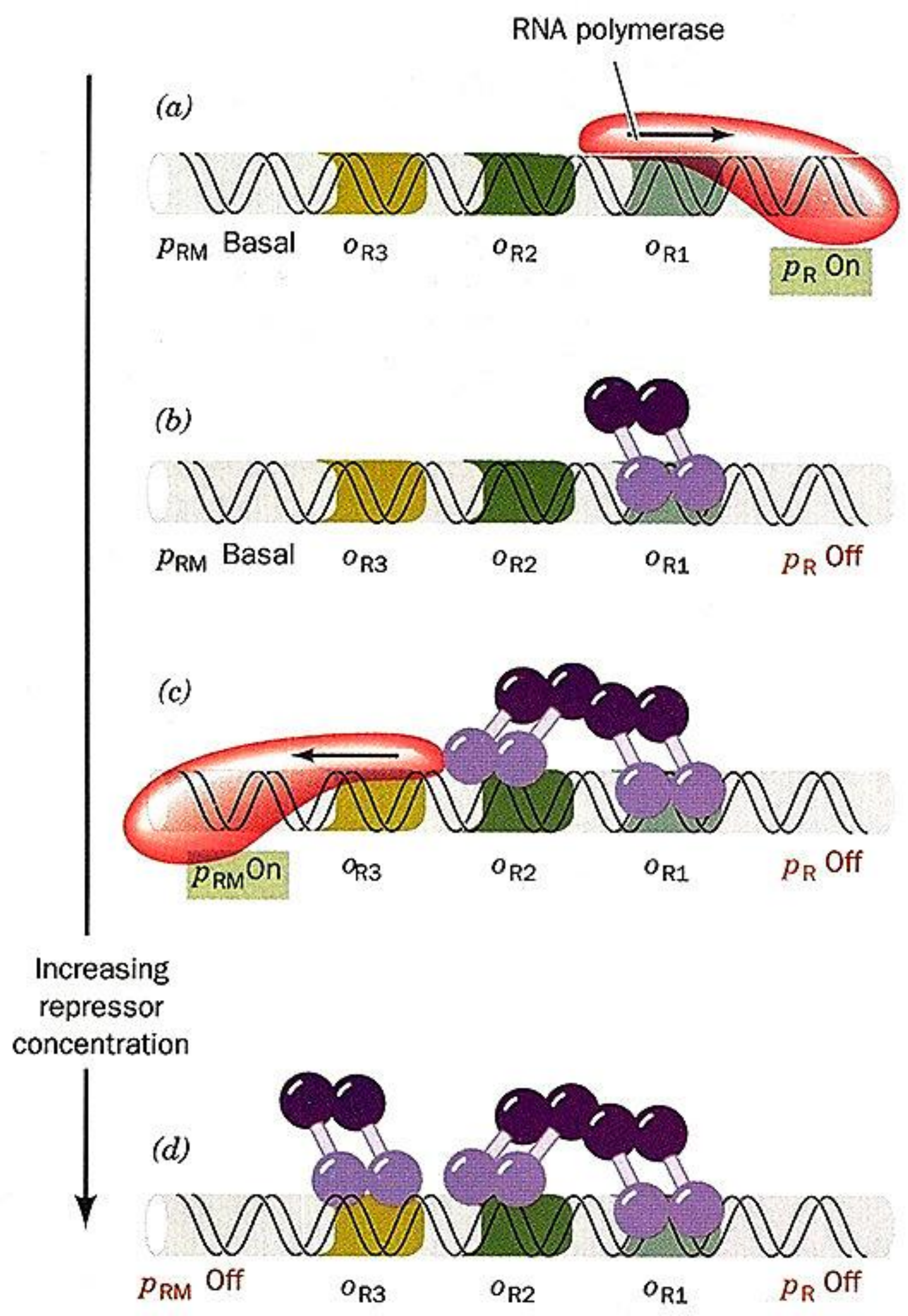
Battle between cI and cro proteins



Repressor type	Repressor conc.	Repressor location			Repressor effect
cI	Low	–	+	+	Activates P_{RM}; represses P_R
cI	High	+	+	+	Represses P_{RM} and P_R
cro	Low	+	–	–	Represses P_{RM}
cro	Intermediate	+	+	–	Represses P_{RM}, P_R, and P_L
cro	High	+	+	+	Represses P_{RM}, P_R, and P_L

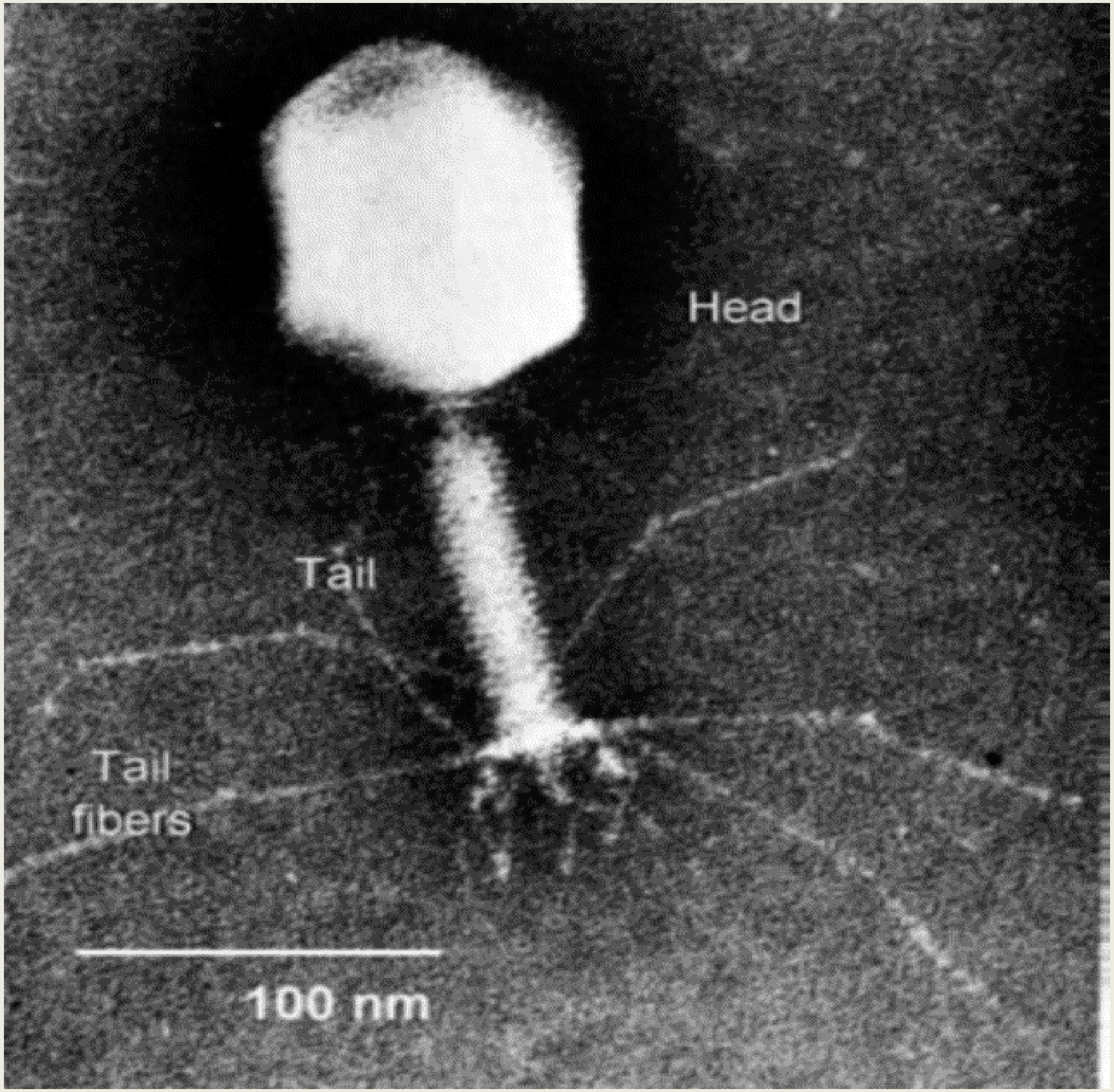
CI protein can enhance its own transcription

Allows RNA pol to enter at PRM



T-even phages

- Large DS DNA Genomes



Genome:
168,000 bp DS DNA
Circularly permuted.
Terminal repeated sequences.

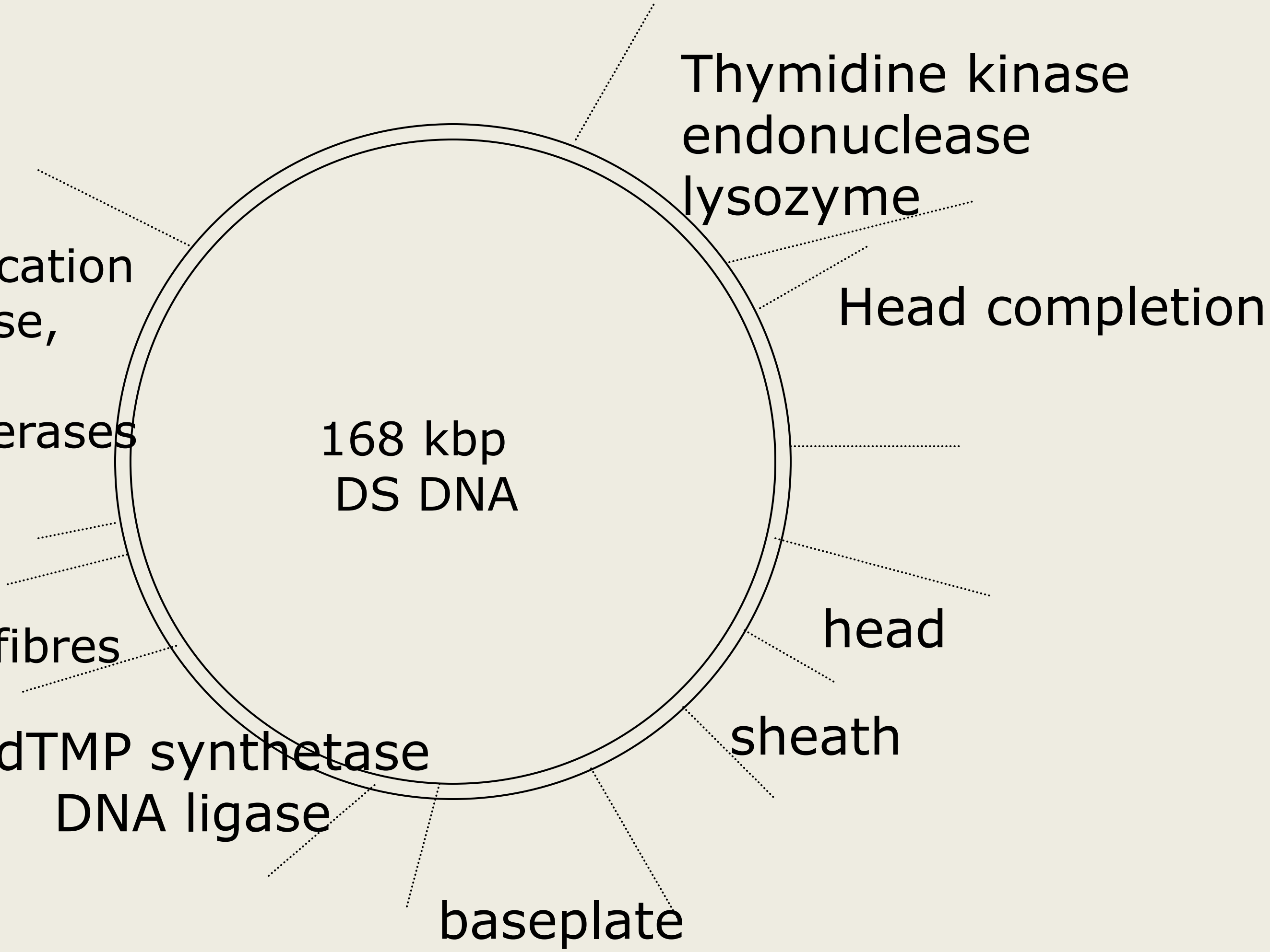
Special nucleotide in genome:
5-hydroxy-methyl cytosine
(instead of thymidine).

Many tail fibres

Bacteriophage T4

http://www.res.bbsrc.ac.uk/mirror/auz/ICTVdB/43010001.htm

Phage T4 genome map - circular genes in clusters; essential and non-essential



Thymidine kinase
endonuclease
lysozyme

Head completion

head

sheath

baseplate

dTMP synthetase
DNA ligase

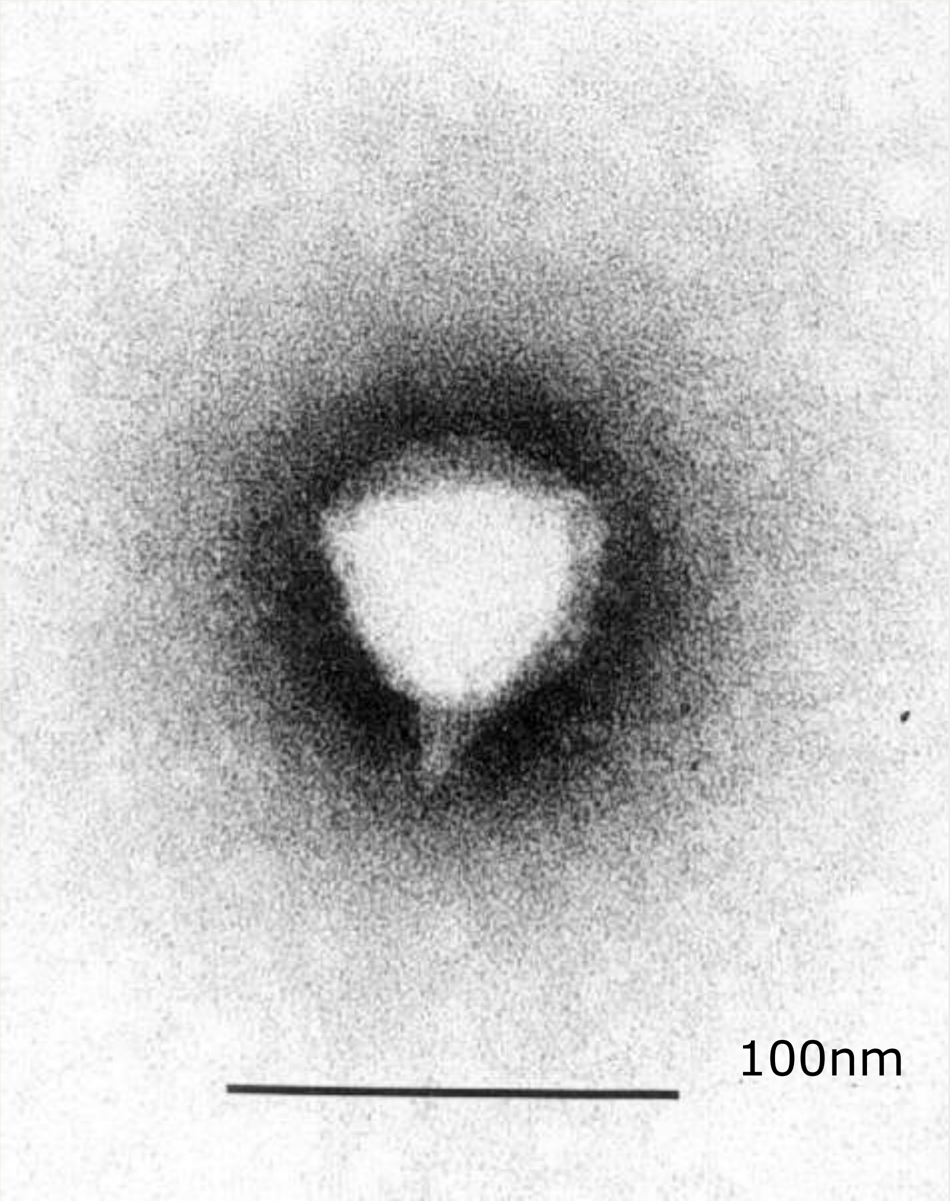
Tail fibres

DNA replication
polymerase,
primase
topoisomerases

168 kbp
DS DNA

EARLY
MIDDLE &
LATE GENES

Transcription from both strands



Bacteriophage T7 Family

(T-odd coliphages)

Genome:
40,000 bp DS DNA
(non permuted)

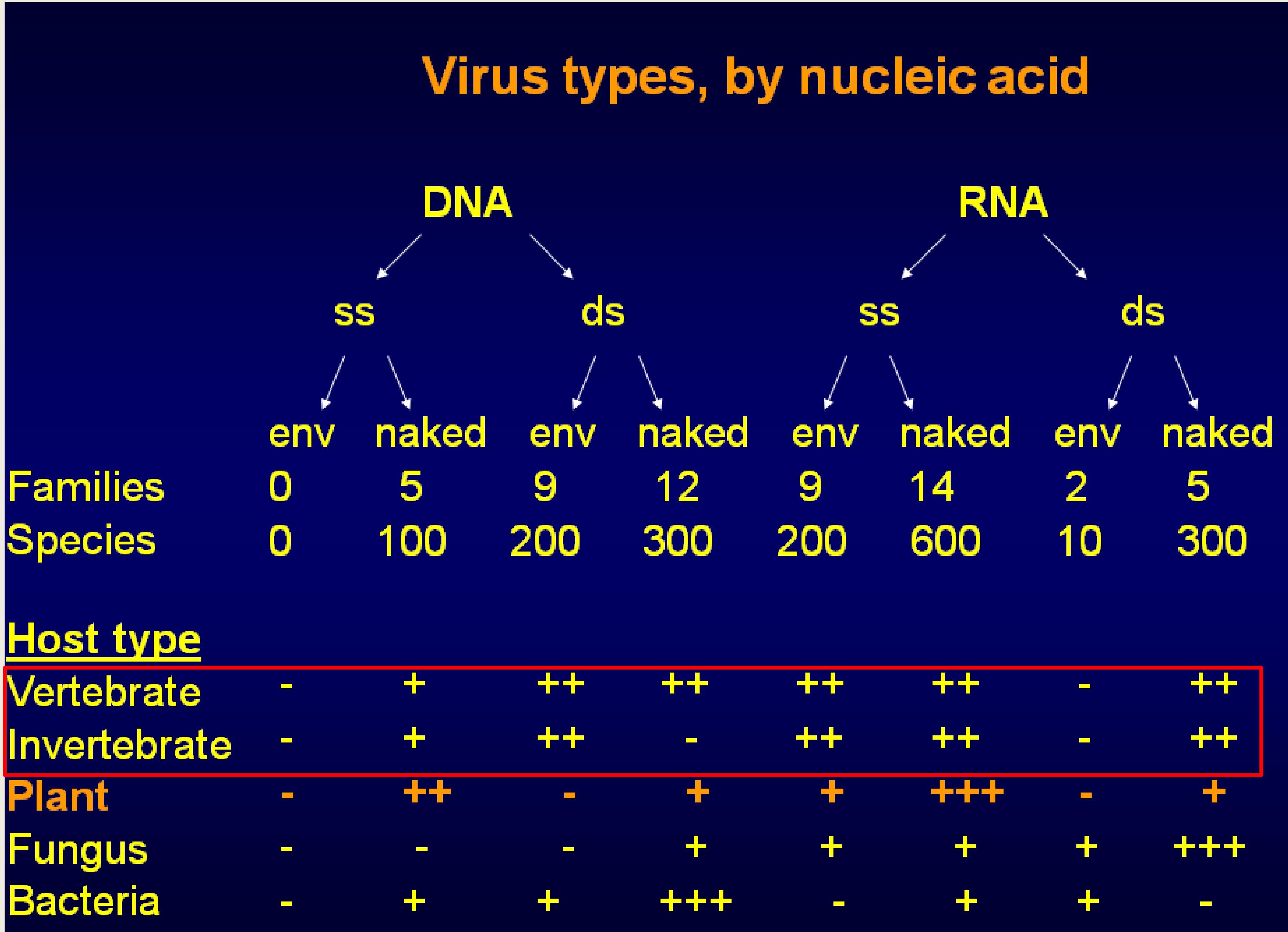
T7 is a lytic phage, and
destroys *E.coli* cells
in approximately 25 min

http://life.anu.edu.au/viruses/Images/Ackerman/Tailedph/Podoviri/402-06.htm

Классификация вирусов по типу хозяина и НК: вирусы животных

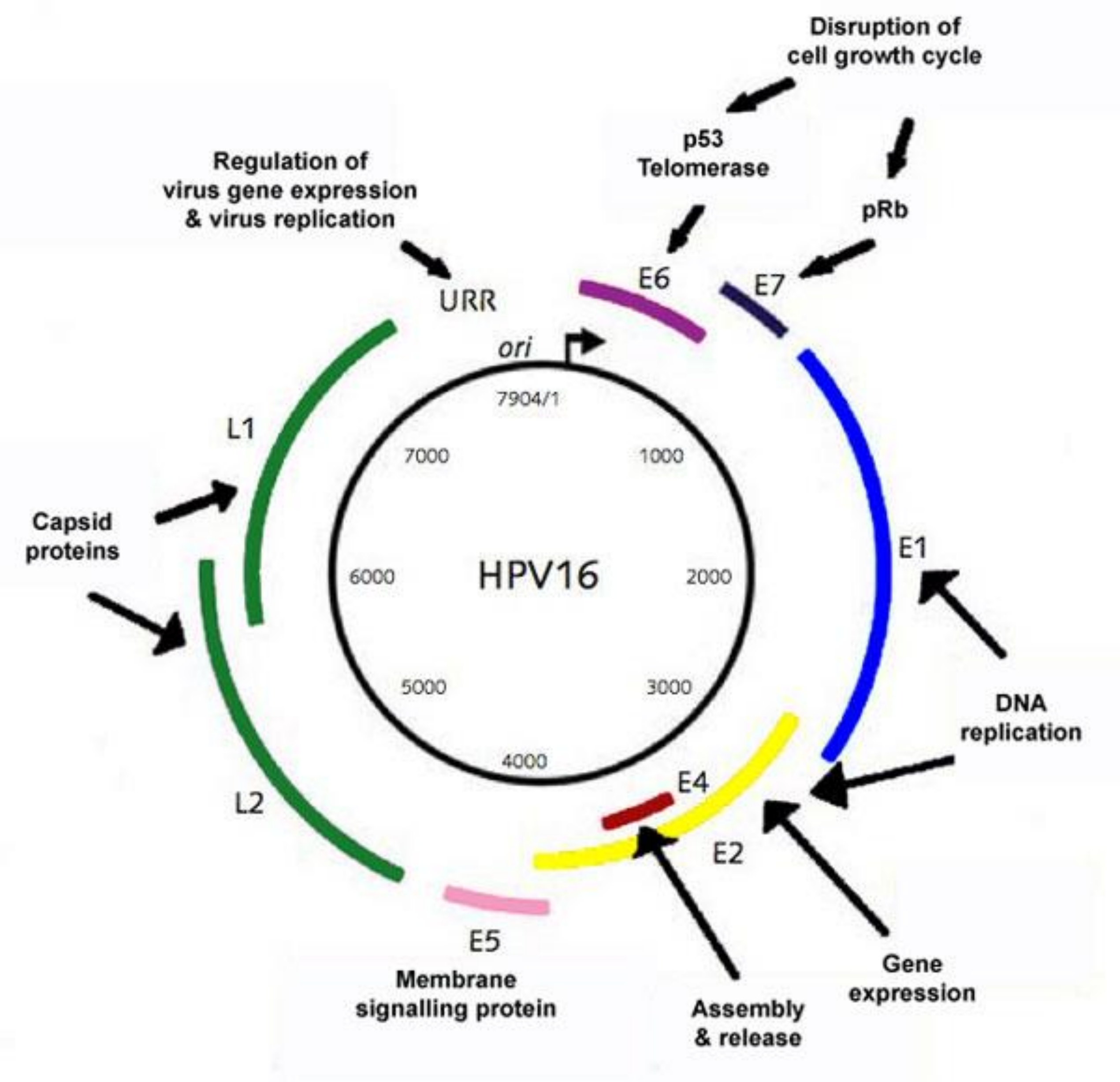
- dsDNA (Adenoviridae, Herpesviridae, Papovaviridae, Poxviridae)
- ss-DNA (Parvoviridae)
- ds-RNA (Reoviridae)
- ss-RNA (Arenaviridae, Orthomuyxoviridae, Paramyxoviridae, Picormnaviridae, Phabdoviridae, Retroviridae)

2002



Virus types, by nucleic acid

	DNA				RNA			
	ss		ds		ss		ds	
	env	naked	env	naked	env	naked	env	naked
Families	0	5	9	12	9	14	2	5
Species	0	100	200	300	200	600	10	300
Host type								
Vertebrate	-	+	++	++	++	++	-	++
Invertebrate	-	+	++	-	++	++	-	++
Plant	-	++	-	+	+	+++	-	+
Fungus	-	-	-	+	+	+	+	+++
Bacteria	-	+	+	+++	-	+	+	-



Papovaviridae:

The papillomavirus genome consists of circular, d/s DNA ~8kbp in size, **associated with cellular histones** to form a chromatin-like substance.

Классификация вирусов по типу хозяина и НК: вирусы растений

- dsDNA (Cauliflower mosaic virus)
- ss-DNA (?)
- ds-RNA (Bromovirus; Cucumovirus; Luteovirus; Nepovirus; Potexvirus; Tobacconecrosis virus; Tymovirus; Watermelon mosaic virus)
- ss-RNA (Potyvirus - potato virus Y; Tobamovirus –tobacco mosaic virus; Tobravirus (+ genome))

2002

Virus types, by nucleic acid

	DNA				RNA			
	ss		ds		ss		ds	
	env	naked	env	naked	env	naked	env	naked
Families	0	5	9	12	9	14	2	5
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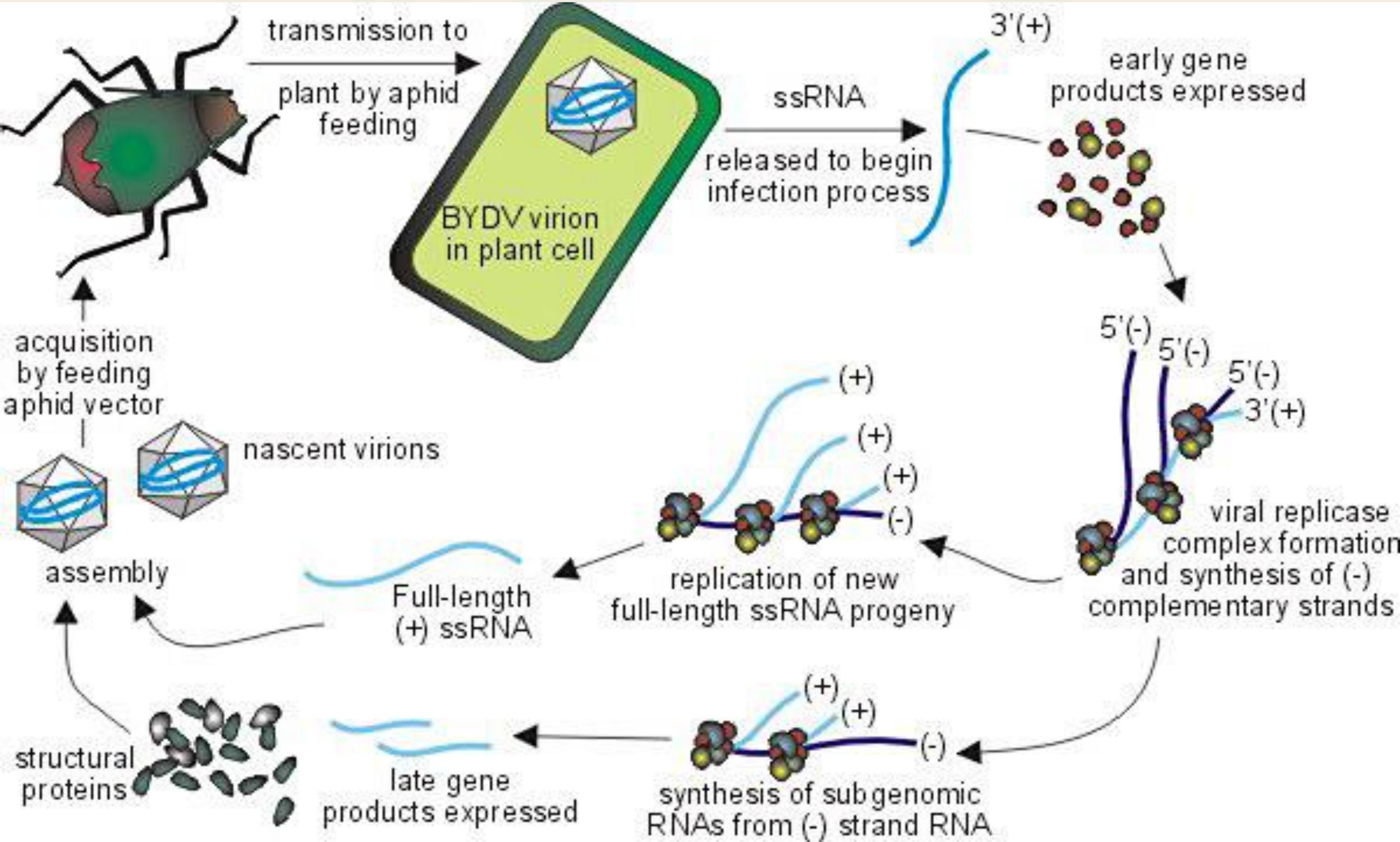
Host type								
Vertebrate	-	+	++	++	++	++	-	++
Invertebrate	-	+	++	-	++	++	-	++
Plant	-	++	-	+	+	+++	-	+
Fungus	-	-	-	+	+	+	+	+++
Bacteria	-	+	+	+++	-	+	+	-

Viral Diseases

- > 400 viruses infect plants; few are economically important pathogens
- The infection remains forever
- Viruses are transmitted from plant to plant by living factors: insects, mites (клещ), fungi and nematodes
- Or non-living factors: rubbing (трение), abrasion or other mechanical means (including grafting (пересадка, прививка) or other forms of vegetative propagation)
- Occasionally transmitted in seed.

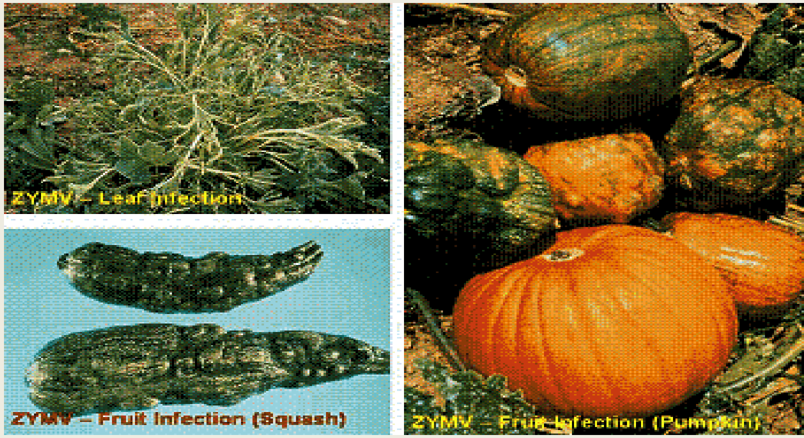
- ***Barley yellow dwarf virus***

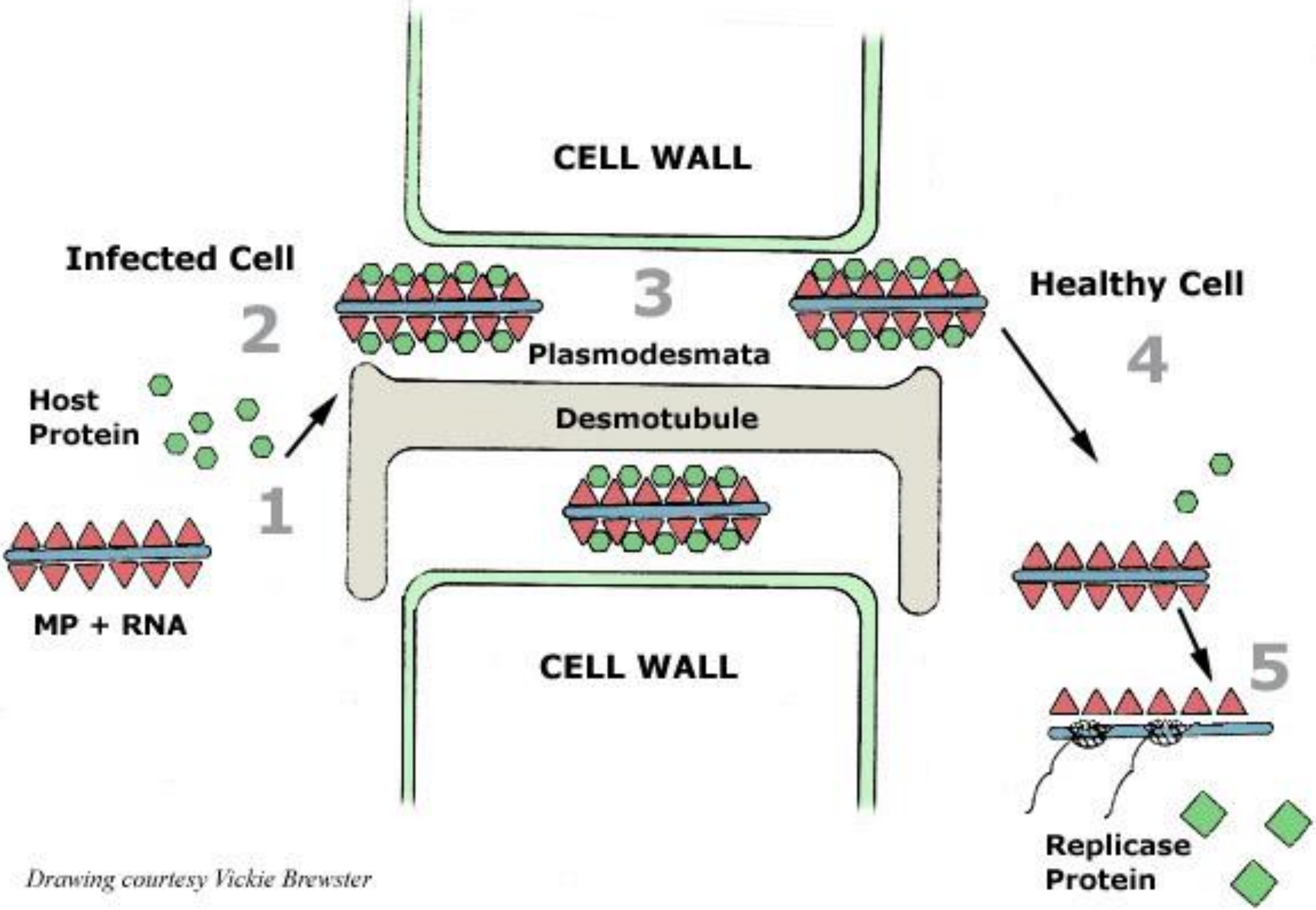

transmission to plant by aphid feeding
BYDV virion in plant cell
ssRNA released to begin infection process
3'(+)
early gene products expressed
5'(-)
5'(-)
5'(-)
3'(+)
viral replicase complex formation and synthesis of (-) complementary strands
(+)
(+)
(+)
(-)
replication of new full-length ssRNA progeny
Full-length (+) ssRNA
(+)
(+)
(-)
synthesis of subgenomic RNAs from (-) strand RNA
late gene products expressed
structural proteins
assembly
nascent virions
acquisition by feeding aphid vector

Virus Disease Symptoms

The symptoms of most virus diseases can be put into ***four*** categories:

1. Lack of chlorophyll formation in normally green organs
2. Stunting or other growth inhibition
3. Distortions
4. Necrotic areas or lesions


ZYMV – Leaf infection
ZYMV – Fruit infection (Squash)
ZYMV – Fruit infection (Pumpkin)



Drawing courtesy Vickie Brewster

Viroids

- Very small, covalently closed, circular RNA molecules capable of autonomous replication and induction of disease
- Sizes range from 250-450 nucleotides
- No coding capacity - do not program their own polymerase
- Use host-encoded polymerase for replication
- Mechanically transmitted; often seed transmitted
- More than 40 viroid species and many variants have been characterized
- “Classical” viroids have been found only in plants

Viroid movement

- Traffic within cell through nuclear pores using VirP1, a nuclear localization protein that binds viroid RNA
- Traffic cell-to-cell through plasmodesmata
- Traffic long distance through phloem
- All of these processes are associated with host proteins

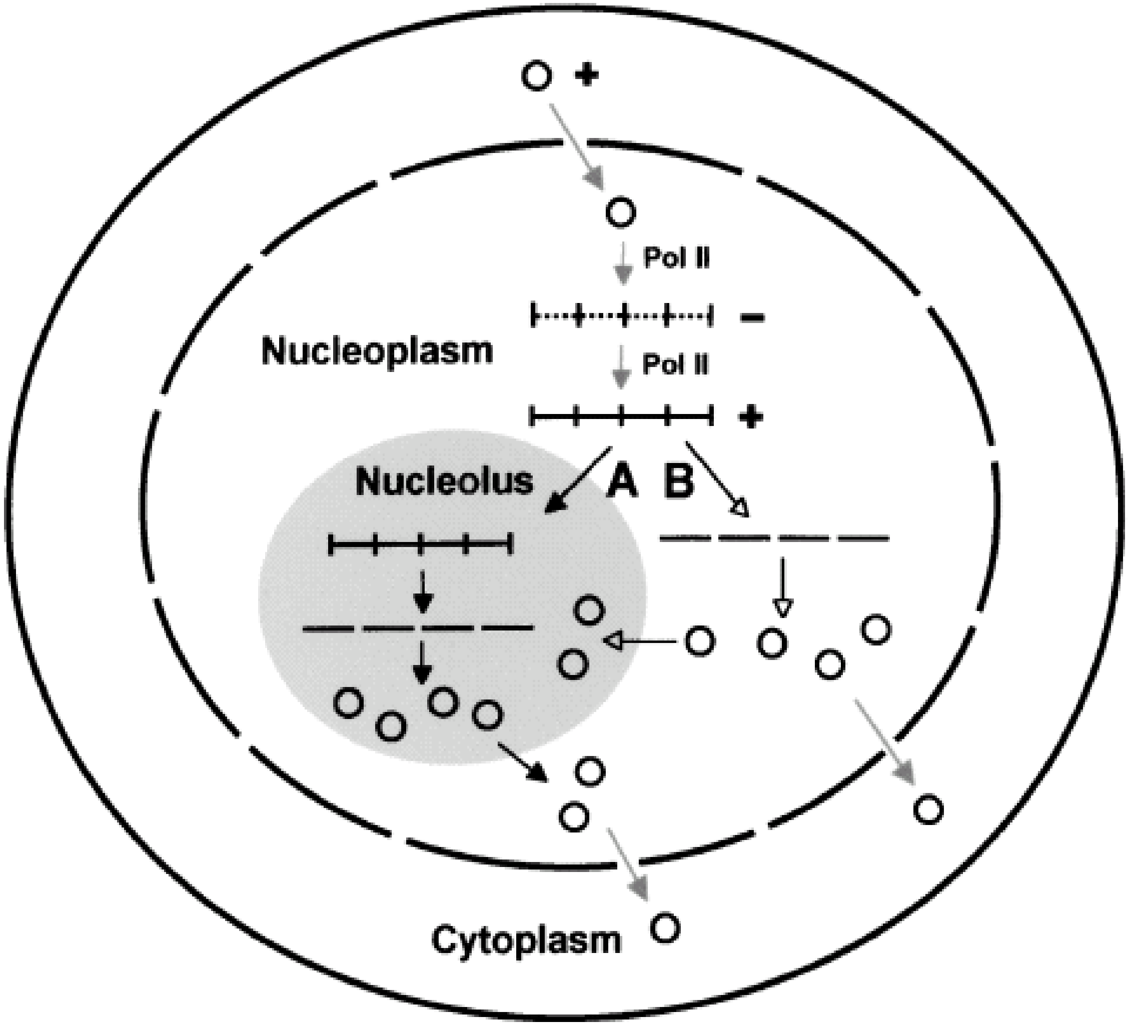


Figure 5. Model of PSTVd Replication Featuring Intranuclear Trafficking of the (+)-Strand PSTVd.

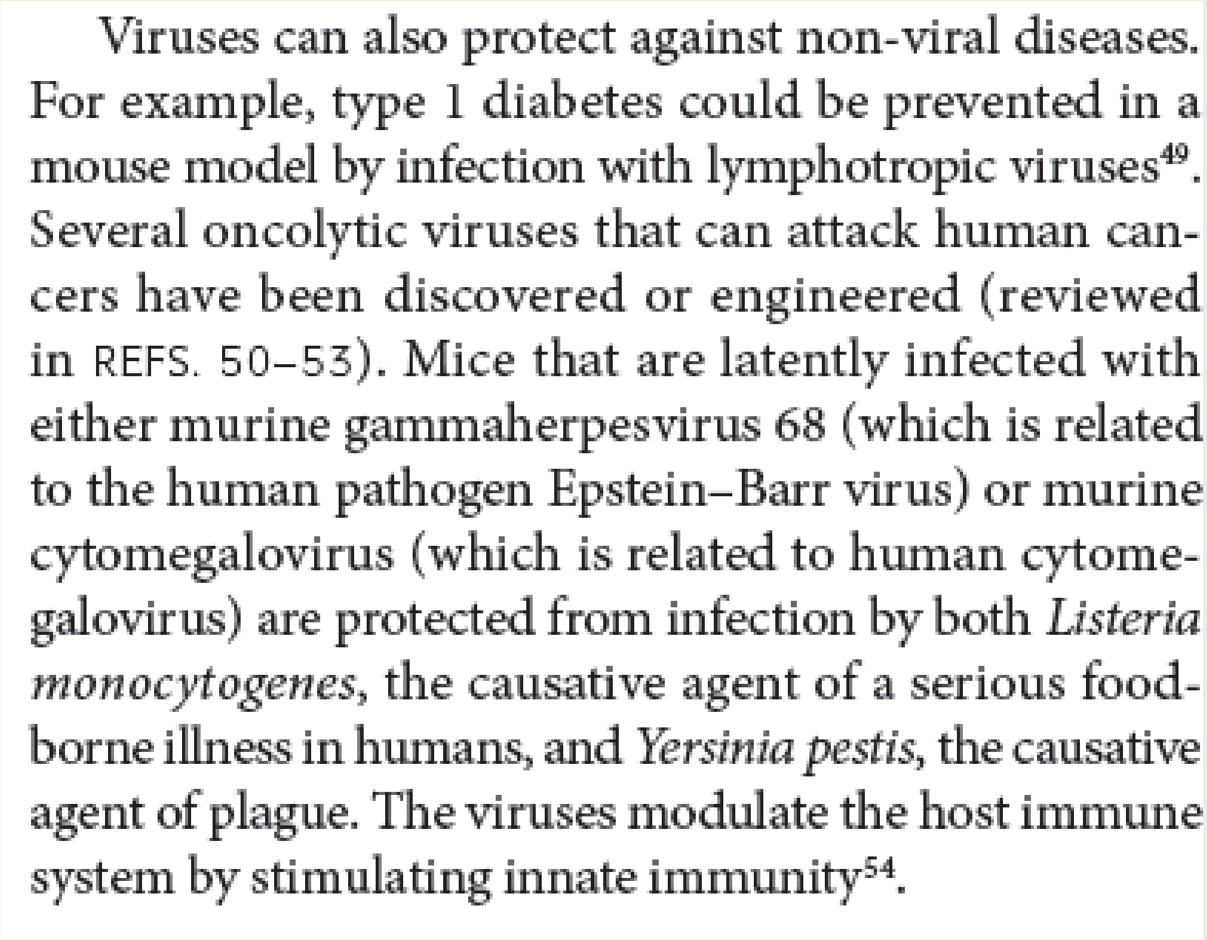
“Good” viruses?

Table 1 | **Types of virus–host mutualism**

Virus group	Hosts	Beneficial effect	Type of mutualism
Polydnaviruses	Parasitoid wasps	Required for survival of the wasp egg in its insect host	Symbiogenic
Retroviruses	Mammals	Involved in the evolution of the placenta	Symbiogenic
Pararetroviruses	Plants	Protect against pathogenic viruses	Symbiogenic
Herpesviruses	Humans	Suppress HIV infection	Conditional mutualism
	Mice	Protect against bacterial infection	Conditional mutualism
Parvoviruses	Aphids	Required for the development of wings	Conditional mutualism
Phages	Bacteria	Allow the invasion of new territory by killing off competitors	Conditional mutualism
		Allow the invasion of mammalian hosts	Mutualism
Yeast viruses	Fungi	Allow the suppression of competitors	Conditional mutualism
Fungal viruses	Fungi and plants	Confer thermal tolerance to fungal endophytes and their plant hosts	Mutualism
Plant viruses	Plants	Confer drought and cold tolerance	Conditional mutualism

Why are endogenous retroviruses there? One hypothesis is that each one represents a plague-culling event: endogenization may result in immunity to an otherwise lethal virus, so only individuals with the endogenized retrovirus survive[31]. There is some evidence for this

At least some endogenous retroviruses encode functional genes and are thought to be involved in major evolutionary leaps. For example, the evolution of placental mammals probably occurred after the endogenization of a retrovirus[35]. Retroviral envelope proteins (Env proteins) cause fusion of cell membranes, a process that not only allows invasion of oncogenic viruses but also is required for the development of the placental syncytium, an essential part of the barrier that prevents maternal antigens and antibodies getting into the fetal bloodstream. In sheep, the endogenous



Viruses can also protect against non-viral diseases. For example, type 1 diabetes could be prevented in a mouse model by infection with lymphotropic viruses[49]. Several oncolytic viruses that can attack human cancers have been discovered or engineered (reviewed in REFS. 50–53). Mice that are latently infected with either murine gammaherpesvirus 68 (which is related to the human pathogen Epstein–Barr virus) or murine cytomegalovirus (which is related to human cytomegalovirus) are protected from infection by both *Listeria monocytogenes*, the causative agent of a serious food-borne illness in humans, and *Yersinia pestis*, the causative agent of plague. The viruses modulate the host immune system by stimulating innate immunity[54].

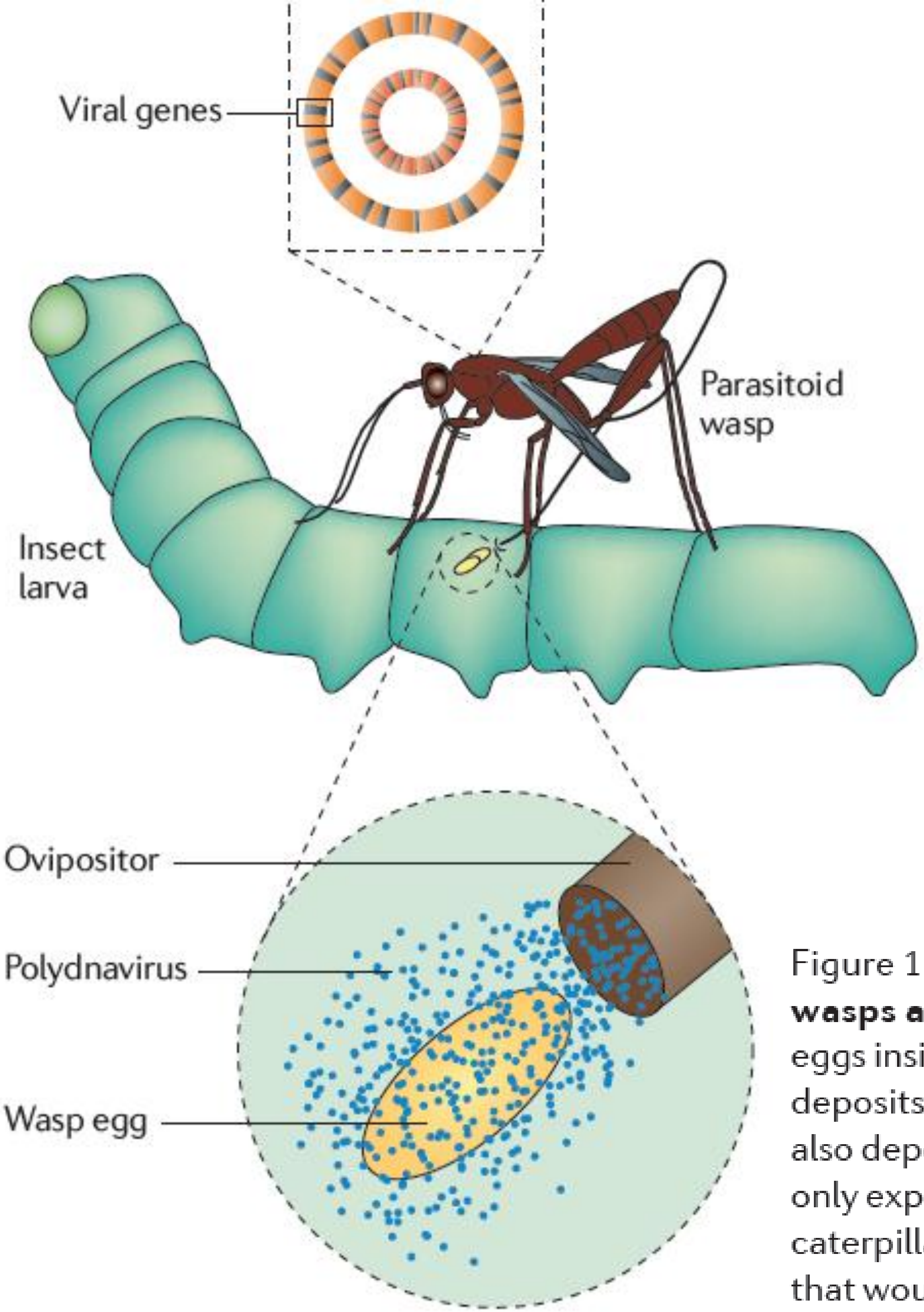
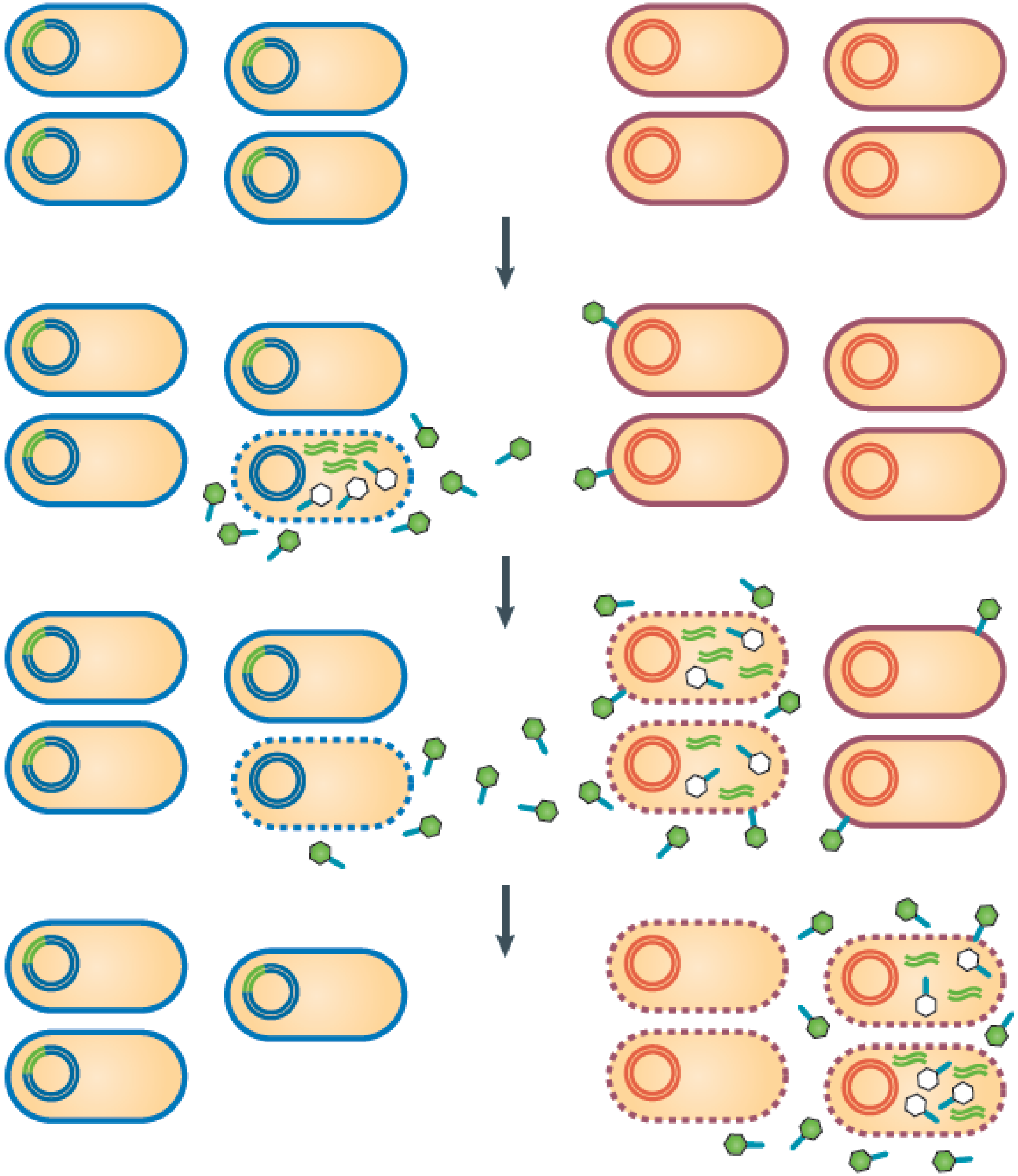


Figure 1 | **The relationship between polydnaviruses, wasps and caterpillars.** Many parasitoid wasps lay their eggs inside a living insect larva. When a female wasp deposits her eggs inside a lepitdopteran caterpillar, she also deposits her symbiogenic polydnavirus virions, which only express wasp genes. These genes are expressed in the caterpillar, where they prevent the encapsulation process that would otherwise wall off and kill the wasp egg.

Viruses as natural weapons



Many bacteria carry a viral genome (green) integrated intro their own genome (blue). These lysogenic viruses remain dormant and render the host bacteria immune to lytic forms of the virus. If the lysogenic virus excises from the genome, it can reproduce rapidly, producing thousands of progeny and leading to the death of the host cell. This releases the viruses into the extracellular environment, where they can kill competing bacteria (red) that are not lysogenic for the virus

Adaptation to extreme environment

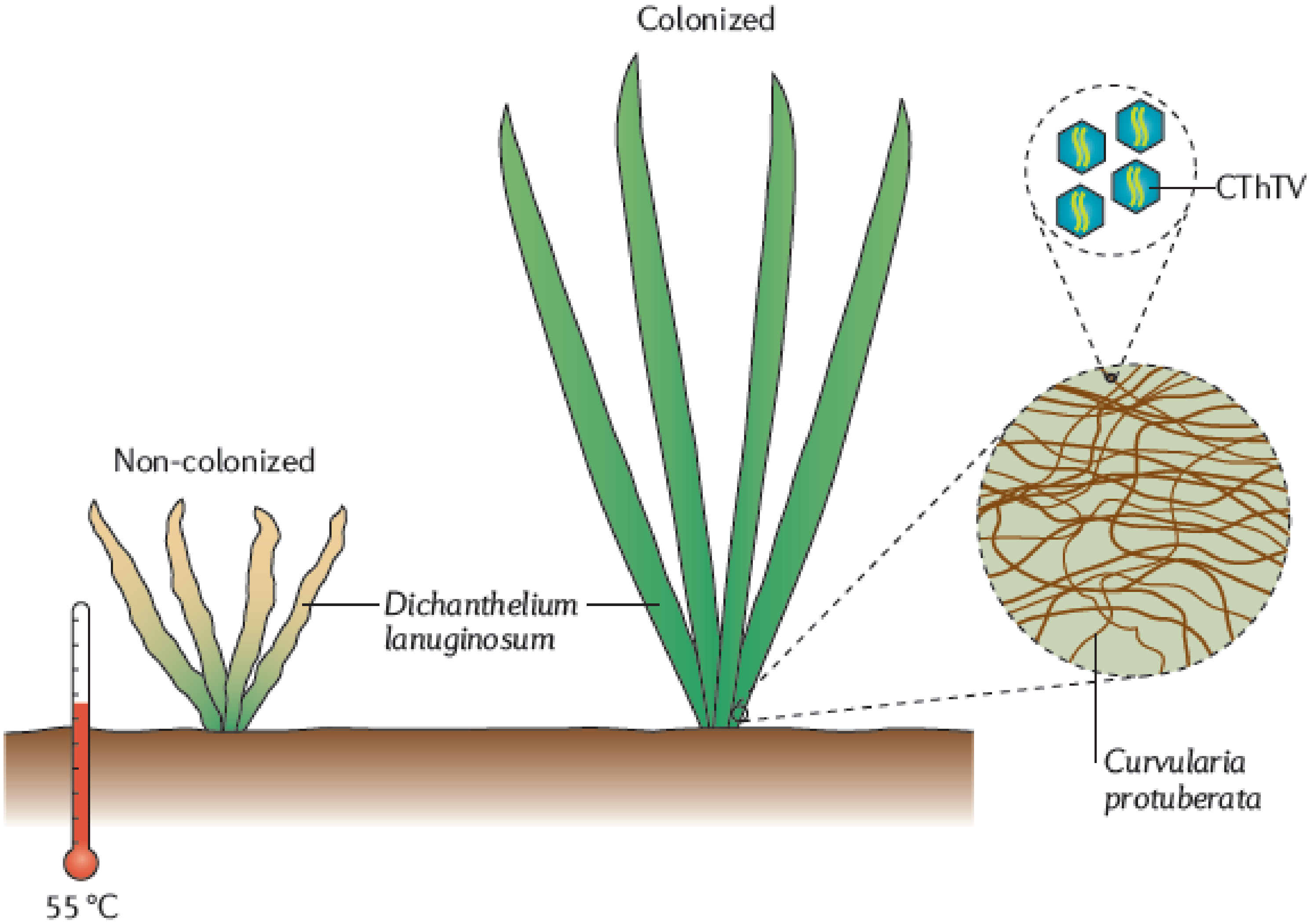


Figure 3 | **A three-way mutualistic symbiosis.** The panic grass *Dichanthelium lanuginosum* is found in geothermal soils in Yellowstone National Park, USA, where it can grow at soil temperatures >50 °C. The plant requires a fungal endophyte, *Curvularia protuberata*, to survive at this temperature. In turn, the fungus requires a virus, Curvularia thermal tolerance virus (CThTV), to confer this thermotolerance effect.